VOL. 8 No. 4 OCTOBER, 1951

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BRITISH JOURNAL OF INDUSTRIAL MEDICINE

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LONDON
BRITISH MEDICAL ASSOCIATION
TAVISTOCK SQUARE, W.C.1

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Brit. J. industr. Med., 1951, **8**, 199.

THE WORK OF THE INTERNATIONAL LABOUR ORGANIZATION IN OCCUPATIONAL HEALTH

BY

A. GRUT

From the I.L.O., Geneva

The knowledge that certain occupations may lead to disease is probably as old as these occupations, but the first comprehensive effort in occupational medicine was made by Ramazzini in 1700, and the active prevention of occupational diseases began much later.

Activities on an international scale were first instituted at the Congress of the International Working Men's Associations in 1867, and from 1890 various congresses dealt with protective regulations and legislation.

The Permanent International Commission for the Study of Industrial Diseases, founded in 1906, has organized nine international congresses in European cities. The conception of health protection through the united efforts of several countries was, therefore, not new when the International Labour Organization, established in accordance with the Treaty of Versailles, subsequently set up an Industrial Hygiene Division.

Activities of the International Labour Organization

The International Labour Organization is a specialized agency in relationship with the United Nations, and comprises the International Labour Conference, the Governing Body, and the International Labour Office.

The Conference, which meets annually, is composed of national representatives of government, management, and labour. This tripartite representation is an essential feature of the Organization. Its principal function is to formulate international labour standards in the form of Conventions and of Recommendations. It may also record its decisions in the form of resolutions. In addition to the general sessions, regional conferences are held.

The Member States are required to submit Conventions adopted by the Conference to their competent national authorities for possible ratification. If a country ratifies a Convention it is obliged to see that its own legislation is brought into accord with the Convention's provisions, and to report annually on the legislative measures which have been taken. Recommendations, on the other hand, are not subject to ratification, but States are obliged to consider them with a view to realizing their provisions by legislative or other action. Members of the Organization are required to report periodically on the position of their law and practice in relation to unratified Conventions and to Recommendations.

The Governing Body is also tripartite in its structure. Its functions include the framing of the Conference agenda, and the general supervision of the work of the Office, and of the various Committees of the Organization.

The International Labour Office provides the secretariat of the Conference ; it prepares documents concerning items on the agenda of the Conference and of the Governing Body, collects and distributes information, and on request furnishes technical assistance to governments, conducts such special investigations as may be ordered by the Conference or the Governing Body, and provides machinery for ensuring the effective application of Conventions. A number of committees and panels of experts have been set up under the Organization. There are, for example, eight committees, appointed since the last war, which deal with specific problems in different industries. These are called the Industrial Committees. Other I.L.O. bodies, which represent industries or occupations, are the Joint Maritime Commission, the Permanent Agricultural Committee, the Committee on Work on Plantations, and the Advisory Committee on Salaried Employees and Professional Workers. These committees, established on a tripartite basis, provide the Office with direct information about the problems in these various occupations, and at the meetings, practical measures for remedying unsatisfactory conditions can be discussed.

Recently a Joint Committee on Occupational

Health has been established with the World Health Organization.

The International Labour Organization has collected data and documents concerning every aspect of occupational health; this information has been disseminated directly by correspondence or by publications; international regulations in the form of Conventions have been established, and Recommendations and Resolutions have been made. International meetings of experts on special subjects have been convened in order to pool the available knowledge and to promote international research.

To assist the Office in these many functions, an expert advisory committee, called the Correspondence Committee on Industrial Hygiene, was established by the Governing Body in pursuance of a resolution of the First International Labour Conference. Subcommittees on Fatigue and on Silicosis have also been set up as the need arose. The members of these Committees are appointed by the Governing Body, and are chosen entirely on the basis of their technical knowledge. No attempt has been made to give representation to various interests on these committees.

Information Service

Direct Assistance.—This service has been given by correspondence in reply to requests from research workers, national organizations, and other persons or bodies dealing with occupational health.

The variety of these written requests for assistance received is indicated by the following list of answers sent out during the last two years to various countries: comments on industrial hygiene clauses in health codes to Costa Rica and to Turkey; advice on the text of an Industrial Hygiene Code to Iran; a list of industrial hygiene authorities in various countries to Czechoslovakia; information regarding the health of workers in various industries to Pakistan and to Uruguay; data on health of workers engaged in tunnelling to Italy; and the health of workers in water-front occupations to New Zealand; data about the incidence of various occupational diseases, such as deafness, to Argentina, and cancer, to France; a report on various hazards, such as those associated with the handling of cement, to Switzerland; the use of coated electrodes to Morocco, and of dangerous radiations to Italy and to the U.S.A.; answers to questions about the toxicity of various chemicals have been sent to Egypt, the Netherlands, Switzerland, and the United Kingdom; and information about occupational health legislation in various industries has gone to Chile, Germany, Iran, Japan, Poland, and the United Kingdom. Data concerning various industrial hygiene methods and their application, such as dust suppression in the hemp industry, were sent to Tanganyika, and data concerning the use of colour in factories to Switzerland.

Publications.—A number of Office reports have contained information on occupational health.

Reports to the League of Nations.—Members of the Correspondence Committee have regularly contributed to the Year Book published by the Health Section of the League of Nations on the progress effected in occupational health. The Office prepared a study on the use of toxic substances in disinfestation in agriculture and horticulture, which was communicated to the League of Nations.

Reports to the United Nations—A report to the United Nations on the activities of the Office is published yearly.

Reports for Conferences and Meetings of the I.L.O.—The contribution to the Director-General's report to the International Labour Conference describes the general trends in occupational health developments in the past year, and mentions special achievements and legislation.

In reports for Regional Conferences the trends in the specific region are described.

The establishment of the Industrial Committees facilitated contact with employers and workers in matters of occupational health. The Office has prepared studies on health conditions in the building, chemical, iron and steel, and textile industries, and in the metal trades.

Bibliography.—From the outset, all bibliographical references were indexed, and published in the *International Labour Review* until 1923, when the increasing volume necessitated separate publication in the *Bibliography of Industrial Hygiene*, which appeared quarterly from March, 1923, to September, 1939. Two additional numbers, published in 1944 and 1945, covered the publications up to 1941. This publication was resumed in 1948 under the title of *Bibliography of Occupational Medicine*, the first two numbers of which appeared yearly. From 1950 it was again published quarterly.

This publication lists each year about 4,000 titles of books and articles on occupational health. The titles are given in the original language. A translation into English and French is given of those titles not in English, French, Spanish, or Italian. The number of pages of each item indicates its volume, and a detailed system of headings gives the context of the articles.

A number of national periodicals give annotated bibliographies, but the number of items is small compared with the *Bibliography*, which is the only

existing publication giving a comprehensive list of the year's publications on occupational health, grouped according to subjects, with cross references, and containing also a detailed subject index.

Technical Monographs: Studies and Reports, Series F.—Several of these publications resulted from studies undertaken in connexion with international regulations—five publications on the use of white lead in painting, two on anthrax. Four, the result of the international conferences on silicosis, included records of the conferences, a bibliography on pneumoconiosis, and an account of workmen's compensation for silicosis in the Union of South Africa, the United Kingdom, and Germany. Some monographs were prepared for meetings attended by the Office, and included for example, *Industrial Hygiene and Safety and the International Labour Organisation*; while others were reports of such meetings, for example, *Medical Inspection of Labour*, which reported the meeting of medical inspectors of factories in Düsseldorf in 1926.

The Encyclopedia *Occupation and Health*.—The International Labour Conference held in Washington in 1919 requested the Office to establish a list of unhealthy industrial processes. In view of the constantly changing hazards in industry it was decided to publish an encyclopedia of occupational health, which was to interpret the words "unhealthy processes" on a broad basis, so as to include "toxic, infectious, parasitic, and all other causes likely to endanger or affect prejudicially the workers' health, life or morals". The material in this encyclopedia was to be grouped under (1) the work, (2) the worker, and (3) the place of work; and assistance in the preparation of the encyclopedia was to be sought from members of the Correspondence Committee, as well as from 95 external collaborators.

This encyclopedia of hygiene, pathology, and social welfare, entitled *Occupation and Health*, in two volumes totalling 2,300 pages, and comprising 410 articles, was published from 1930–34 in English and French.

The articles give technical descriptions of industrial processes, references to industrial uses, the causes of risks, pathology, clinical data, prophylaxis, statistics, and current legislation. Other articles deal with occupational diseases of the special systems, infections, etc., and finally there are comprehensive articles on environmental conditions, such as ventilation, heating, lighting, dust elimination, sanitation, etc. Supplements, published from 1938–40, contain articles on new processes or products, and revisions of earlier articles.

This publication describes industrial processes, whereas the usual textbooks are confined to descriptions of the diseases, or in the case of toxicologies, to descriptions of the toxic products. It gives the international aspect of the problem, thereby furnishing information which cannot easily be obtained elsewhere. It seems safe to say that the encyclopedia has been widely employed and, in spite of its age, is still used when the fundamental aspects of a problem are studied. It is now out of print, but a new edition is envisaged.

International Meetings of Experts

Meetings of Correspondence Committee.—Before the war, the Correspondence Committee on Industrial Hygiene held regular meetings to discuss reports on current problems prepared by the Office. The meetings passed resolutions which were either brought before the Governing Body, or were referred to the Office, or to special committees for further study. Questions to be treated by the International Labour Conference with a view to the establishment of international regulations (e.g., on workmen's compensation) were always discussed previously at one or more sessions of the Committee. To give an idea of the functions of this Committee, some of the subjects with which it has dealt are listed: medical inspection of factories (1924 and 1934); colour vision tests (1924); anthrax (1922–30 1934); colour vision tests (1924); anthrax (1922–30); industrial physiology (fatigue) (1926); injuries due to *x*-rays and radio-active substances (1926); frequency of periodical medical examinations (1926); hydrocyanic acid (1928, 1936); rationalization (1931); poisoning by solvents (1931 and 1933); nutrition in industry (1932 onwards); standard code of industrial hygiene (1928, 1933); employment of older workers (1933); manganese poisoning (1934); medical service in industry (1934); ocular service in industry (1934); standardization of radiographic methods in silicosis (1934); asbestosis (1935); infection from dust in the marketing and sorting of rags (1935); occupational dermatitis (1935); work in caissons (1935); labelling of containers of toxic substances (1934 and 1936); compensation for various occupational diseases (1926–36); miner's nystagmus (1936); ankylostomiasis (1936); disinfestation in agriculture and horticulture (1936); code for office work (1936); training in industrial medicine (1936); and statistics of occupational diseases (1936).

International Conferences of Experts.—Three International Conferences of Experts on Pneumoconiosis have been held, in Johannesburg (1930), in Geneva (1938), and in Sydney (1950). The two first

conferences dealt mainly with silicosis. These Conferences have been of international importance in pooling the available information on the pathogenesis, clinical aspects, and diagnosis of pneumoconiosis and on the various preventive measures. The Conferences have also furthered national legislation on compensation for disability caused by pneumoconiosis.

The inscription of silicosis in the international schedule of compensatable diseases was a direct result of the Johannesburg Conference. The Sydney Conference discussed the incidence of pneumoconiosis in various countries, especially of coal miners' pneumoconiosis; the value of routine tests in determining disability; the diagnostic methods, especially in radiology, where a project for international classification of radiographs in some pneumoconioses was established; measures of treatment and rehabilitation, etc. The record of the Conference is now being prepared.

International Regulations

Several decisions of the International Labour Conference relate to aspects of occupational health: Recommendation on white phosphorus (1919); Convention on the use of white lead in painting (1921); Conventions on workmen's compensation (1925 and 1934); Recommendation on medical care (1944); Conventions on sickness insurance in industry and agriculture (1927); a number of Conventions, Recommendations, and Resolutions on the protection of women and young workers; and a Convention and a Recommendation on labour inspection (1947).

In addition, the many Resolutions of the Correspondence Committee, approved by the Governing Body, dealt with such subjects as duties of the factory doctor (1924); periodicity of medical examination (1926); medical inspection in factories (1934); protection against anthrax (1930); regulation of work in caissons (1935); compensation for various occupational diseases (1935); and the labelling of toxic substances (1935).

The protection of the health of workers in places of employment is on the agenda of the 1952 Session of the International Labour Conference, and may be the object of international regulations.

Lead Poisoning.—A Recommendation was adopted in 1919 whereby women and young persons should be excluded from various occupations involving exposure to lead, and that where employment of women and young persons was permitted, such employment should be subject to certain conditions dealing, *inter alia*, with ventilation, cleanliness of workrooms, notification of cases of poisoning, periodical medical examination, washing facilities, and special protective clothing.

The Convention on white lead adopted by the International Labour Conference in 1921 prohibited the use of white lead or sulphate of lead in internal painting, making its use subject to regulations. The employment of women and young persons in any painting work of an industrial character involving the use of these pigments was prohibited.

To facilitate the ratification of the Convention, the Office, in 1927, published a comprehensive account of the medical and technical aspects of lead poisoning and its prevention with gratifying results as to ratification. Twenty-seven countries have now ratified this Convention.

Phosphorus Poisoning.—In 1919 the Conference adopted the Recommendation that each Member State which had not already done so, should adhere to the International Labour Convention adopted at Berne in 1906 on the prohibition of the manufacture, importation, and sale of matches containing white phosphorus. At the present time, this Convention is in force in 34 States.

Anthrax.—The question of anthrax illustrates the difficulty of reaching international agreement on the practical application of preventive measures.

An international commission had studied the disinfection of hides and skins as early as 1908, and in 1919 the International Labour Conference adopted a Recommendation on disinfection of wool affected with anthrax spores. At that time this last question was being studied by a Committee appointed by the British Government, and a method was worked out, and put into operation on a commercial scale. However, when the question was discussed at the International Labour Conference in 1921, with a view to the adoption of a Convention, further study was considered necessary, and the question was referred to an Advisory Committee. This Committee was of the opinion that in most countries the principal danger of anthrax arose from the manipulation of hides and skins. A Mixed Subcommittee with the League of Nations was established, which directed research designed to discover effective methods of disinfection which would not injure the materials being handled.

In 1924 the International Labour Conference saw no prospect of arriving at an international agreement concerning the question of disinfection of wool and hair, and referred the other questions to the Correspondence Committee. As the research instigated by the Mixed Subcommittee had not, in 1928, reached a stage at which the results could be applied industrially, and large-scale experiments in

tanneries were impossible to effect with the means available, the Correspondence Committee proceeded to formulate Draft Regulations for Protection against Infection of Anthrax in the Hides and Skins Industry. These regulations, dealing with the hygiene of work places, personal hygiene of the workers, and notification of cases of anthrax, were approved by the Governing Body in 1931.

In addition to the drafting of these regulations, progress was made by the publication of statistics on anthrax, by the furthering of veterinary control of infected flocks, and by contact with appropriate national organisations.

Medical Inspection of Factories.—The Factory Inspection Recommendation in 1919 advocated the establishment of a system of factory inspection including a service for safeguarding the health of the workers. The scope of inspection, the nature of the functions and powers of inspectors, and the organization of inspection, were elaborated in a Recommendation in 1923.

The Correspondence Committee in 1924 adopted a resolution defining the rights of medical inspectors; in 1926 a resolution on the periodicity of inspections in various dangerous occupations; and, finally, in 1934, a resolution on the duties and requirements of the medical inspectors of factories.

The Convention in 1947 calls for measures to ensure that duly qualified technical experts and specialists, including specialists in medicine, are associated in the work of inspection. A Recommendation, also adopted in 1947, deals with labour inspection in mining and transport undertakings, and with the preventive duties of labour inspectorates in general to ensure protection against unhealthy or dangerous conditions.

Notification and Statistics.—The notification of occupational diseases is ensured by workmen's compensation laws. The Labour Inspection Convention, 1947, contains a provision concerning notification to the labour inspectorate of occupational diseases. It does not, however, establish an obligation on governments to require such notification, but states that the labour inspectorate shall be notified of cases of occupational diseases "in such cases and in such manner" as may be prescribed by national legislation. The same Convention requires the publication of statistics of occupational diseases in the annual report of the factory inspectorate as far as the matter is under the control of that authority. The Labour Inspection Recommendation, 1947, specifies details of such statistics, i.e., the number of cases and a classification according to cause and to industry.

The Seventh International Conference of Labour Statisticians, 1949, considered that the state of development of statistics on industrial injuries and occupational diseases did not justify the drafting of a Convention on the subject which will, however, be discussed at the 1952 session of the Conference.

Medical Training and Health Education.—The Correspondence Committee in 1934 adopted a resolution concerning the training of the personnel of medical inspection services.

In 1939, in a report on training the Office embodied all available data obtained by means of a questionnaire addressed to Member Governments.

The Joint Committee of the I.L.O. and the W.H.O. on Occupational Health, at its meeting in 1950, drew up recommendations on the training of medical students, doctors, nurses, industrial hygienists, and other persons responsible for the health of workers.

Medical Examination.—A Convention was adopted in 1922 concerning compulsory examination of children and young persons employed at sea. In 1946 two Conventions and a Recommendation were adopted concerning medical examination of young persons in industrial and non-industrial occupations, and a Convention on the medical examination of seafarers. The Conventions relating to industry require pre-employment medical examinations to determine physical fitness for employment, and provide for re-examinations until the age of 18 years or, in the case of occupations involving high health risks, until the age of 21.

The Recommendation contains provisions for the treatment of persons found by examination to be suffering from disease.

Vocational Guidance.—A comprehensive Recommendation on vocational guidance was adopted by the Conference in 1949, advocating that appropriate tests of capacity and aptitude, and where so desired, other psychological tests, should be made available for use in vocational guidance as appropriate to the needs of individual cases. It also advocated the development, in cooperation with the appropriate rehabilitation services, of adequate and appropriate arrangements for the vocational guidance of young persons with physical or mental handicaps or limitations, or who manifest personality disorders of such a nature as to prevent, or make particularly difficult, their vocational adjustment.

Industrial Hygiene.—A Standard Code of Hygiene Regulations drafted by the Office was discussed at various meetings of the Correspondence Committee from 1928 onwards, and finally published in 1934.

It contained minimum standards regarding factory construction, cubic space, ventilation, lighting, heating, underground premises, etc., and was intended for the guidance of countries revising or drafting for the first time their Labour or Hygiene Code.

A guide for factory inspectors in their work, *Industrial Environment and Health*, issued in 1936, described industrial hygiene methods.

A *Model Code of Safety Regulations for Industrial Establishments*, published 1949, contains regulations for dangerous and obnoxious substances, dangerous radiations, health protection, personal protective equipment, selection of workers and medical service.

Workmen's Compensation.—Two Conventions (1925 and 1934), and a Recommendation (1928) deal with workmen's compensation. The 1925 Convention contained the first international schedule comprising anthrax and poisoning by lead and by mercury; the second schedule increased the list considerably to a total of 10 diseases or hazards. These Conventions have been ratified by 32 and 22 countries, respectively. Since 1934, schedules in national legislation have superseded the international schedule considerably and a revision of this schedule is envisaged.

Rehabilitation.—Rehabilitation has been the subject of several Office publications, such as *Training and Employment of Disabled Persons*, *Placement of Disabled Persons*, *Rehabilitation of Disabled Persons in the Mining Industry*, and *Rehabilitation of the Tuberculous*.

Three Recommendations (1948, 1949, 1950) deal with employment service organization, vocational guidance, and vocational training of the disabled, respectively.

Collaboration with Other International Agencies

Collaboration with the Health Section of the League of Nations comprised the exchange of information on venereal diseases, prevention of anthrax, occupational cancer, toxic substances in disinfestation in agriculture and horticulture, interchange of medical inspectors of factories, study of activities of medical services of insurance institutions, rural hygiene, and workers' nutrition.

Since 1948 close inter-secretariat collaboration has existed between the Office and the World Health Organization which has recently established a section on Social and Occupational Health. The joint Committee of the I.L.O. and W.H.O. on Occupational Health which has made recommendations on the training of persons responsible for the health of workers has also considered the collaboration between industrial medical and public health services.

The Office has collaborated with the United Nations, the International Refugee Organisation, and the World Health Organization in planning the rehabilitation of disabled displaced persons, and a comprehensive scheme is now being developed for the rehabilitation of the disabled. Collaboration has been initiated with the F.A.O. in the planning of surveys of nutrition of workers in Latin America.

Present and Future Activities

The subject of the objectives and minimum standards of social security, including medical care, was on the agenda of the 1951 Conference, and will possibly be embodied in a Convention.

Revision of the Maternity Protection Convention is envisaged, and the steps to be taken to protect women workers, in view of their roles as mothers and home workers, are being studied by the Office.

Underground work of young persons in mines, which was dealt with in the Safety Code for Underground Work in Coal Mines, is being studied with the view to the drafting of international regulations.

The possibility of establishing international regulations for extending to agriculture the medical examination of young persons under 18 years is under consideration. The Office is also dealing with the following problems.

Recommendations of the Third International Conference of Experts on Pneumoconiosis.—A classification of radiographs in certain forms of pneumoconiosis was established at the Conference, and work on an international basis is progressing. This involves comparisons between the classification of identical radiographs examined by experts in various countries.

The Conference drew attention to the problem of preventing pneumoconiosis in civil engineering undertakings such as tunnelling, etc., and in the handling of grain cargoes, and the Office is studying measures against these hazards.

A directory of specialists in pneumoconiosis is in preparation. The Conference recommended that a future I.L.O. Conference should be held to deal with the prevention of pneumoconiosis mainly from the point of view of the engineer, the physicist, and the chemist.

Protection against Other Health Risks.—The agenda of the 1952 Conference contains the item: protection of the health of the workers in their places of employment.

The Office has prepared a report on the law and practice in various countries including notification, statistics, medical examination, inspection services,

and engineering methods of protection. This report contains a questionnaire which will be circulated to the Member States, and a report based on the replies to this questionnaire will be discussed at the 1953 Conference, and may possibly form the basis of international regulations.

A revision of the international schedule for workmen's compensation is envisaged, as the 1934 schedule is outdated.

Studies on statistical information on the causes of diseases in the chemical industries, on the possibility of classifying chemical substances as dangerous, obnoxious and toxic, on the elaboration of a text on labels of containers of such substances, and finally, on the health of shift workers in the chemical industries, are in preparation for the next session of the Chemical Industries Committee.

The publication of the *Bibliography of Occupational Medicine* which was resumed in 1948 will be continued.

In addition to these activities of disseminating information and establishing international regulations, the Office provides direct advice and assistance, especially under the "Technical Assistance Programme for Under-developed Countries".

General Trends

The scope of occupational health has changed during the time in which the I.L.O. has been active. The activities are at present not limited to prevention of hazards by prohibition or the drawing up of lists of such hazards, nor to payment of compensation for disablement. Occupational health aims at the promotion and maintenance of the highest degree of physical, mental, and social well-being of workers in all occupations.

The achievement of this aim needs action on a large scale: medical supervision of the workers by industrial health centres, provided with the necessary technical equipment, in collaboration with doctors familiar with local conditions. At present, the supervision of small work places, and of rural workers is grossly inadequate.

Legislative measures will probably be necessary, since voluntary health promotion is generally too slow and erratic.

An improvement of the training in occupational health of all those persons responsible for the health of the workers, will require a concerted action by universities, by government health services, and by employers and workers on a national and international scale.

There is still much to be learnt about adaptation to work through job analysis and medical examination of both the healthy and disabled. Industrial psychology has an important application in all relations between the worker and his job, his supervisor, his doctor and his manager, but the worker's greatest need is still a safe working environment.

Health surveys are easy to undertake in industrial populations, but should be undertaken only where a reasonable chance of positive results justifies the expenditure in time and money. All efforts should be mobilized in the pooling of knowledge, and a whole-hearted collaboration between individuals, groups, and nations should be achieved to maintain the productivity and well-being of the worker, for his well-being is one of the chief weapons against unrest and war. In this task the I.L.O. will continue as in the past, to collect and disseminate information on what is being done in the various countries, and to further the adoption of national, and where appropriate, international, measures to promote the health of all workers.

Brit. J. industr. Med., 1951, **8**, 206.

THE WORLD HEALTH ORGANIZATION AND OCCUPATIONAL HEALTH

BY

SVEN FORSSMAN

Lately Consultant on Social and Occupational Health, WHO

It is necessary to have some general knowledge of the work of the World Health Organization (WHO) to understand the position of occupational health within its programme. For this reason a general survey of the work of WHO will be given in the first part of this article, and the second part will deal with occupational health problems.

Survey of Work by WHO

To deal with special problems, the United Nations have organized several specialized agencies such as FAO for food and agricultural problems, UNESCO for education, and WHO as the specialized agency responsible for health problems.

WHO began its activities on an interim basis in 1946, and when the required number of countries had ratified the Constitution in April, 1948, WHO began work on a permanent basis.

The objective of WHO is stated in the Constitution to be " the attainment by all peoples of the highest possible standard of health ". Its definition of health is " a state of complete physical, mental and social well-being ". The prevention of accidents, and the improvement of working conditions are also specifically mentioned in the Constitution of WHO.

WHO includes a headquarters with a permanent staff, an executive board of 18 members, who meet twice a year to follow up the work of headquarters, and an assembly which meets annually to decide the general principles of the organization's work, budget problems and other issues. The headquarters, which is in Geneva, is organized in three departments, which, in turn, are divided into divisions and sections. For the field activity, WHO has divided the world into six regions with regional offices. There is one office for Europe, one for Africa, one for the Middle East with its office in Alexandria, one for South East Asia with an office in New Delhi, one for the American continents where the Pan-American Sanitary Bureau serves as the regional office in Washington, and one region for the Western Pacific where the office will, this year, be permanently established in Manila. There is at present in WHO a tendency to decentralize activity from the headquarters to the regional offices.

The work of WHO may be divided into two main parts: the collecting and compiling of information which is then distributed by various means, and the field work and other activities the function of which is to solve theoretical and practical health problems in various parts of the world.

Much of the information thus collected deals with causes of deaths, epidemics, etc. An international nomenclature on the causes of death has been issued by WHO; new international regulations for quarantine for epidemic diseases have been adopted this year by the World Health Assembly. The section on biological standardization proposes suitable international standards on antibiotics or drugs, and an international pharmacopoeia will be printed this year on the basis of work done at WHO headquarters and by one of its committees of experts.

The information collected and compiled by WHO will be distributed all over the world through several publications: the *WHO News-Letter*, which is in a somewhat popular form, and the more scientific *Bulletin* of WHO and *Chronicle* of WHO, as well as the weekly *Epidemiological Record* and the *Epidemiological and Vital Statistics Report*. WHO is also sending out daily reports by radio on the situation of epidemic diseases in different parts of the world, and this is of great importance to those operating air and sea travel.

Almost every section at headquarters has available a group of experts who can give the necessary information on special problems within each section's scope. A certain number of these experts may form a committee of experts to deal with theoretical health problems, and the reports of these committees provide useful information. There are committees of experts, for instance, dealing with biological standardization, insecticides,

tuberculosis, and mental health. When two specialized agencies have a common interest in a field, a joint committee of experts may be created as, for instance, the Joint FAO/WHO Committee on Nutrition, or the two Joint ILO/WHO Committees on the Hygiene of Seafarers, and on Occupational Health.

On request from a country WHO may begin field work to solve some practical health problem in that country. This may be done by sending experts or groups of experts as consultants or to demonstrate the application of certain health methods. Demonstration areas or health centres may be organized where field work can be done and, at the same time, local health personnel may be trained.

One of the main obstacles to the raising of health standards is, in many countries, the lack of trained personnel. To educate and train health personnel in various countries is one of the most important tasks of the organization. This may be done not only in demonstration areas in the respective countries, but also through fellowships or travel grants to doctors, engineers or nurses for studies at foreign universities, or for travel in other countries. International seminars on health problems, at which a number of highly qualified people can discuss one or several health problems from different points of view, are very effective in stimulating interest and exchanging accounts of experiences. Reports from such seminars provide valuable information on the present situation of the health problems discussed from the research and practical points of view.

When WHO began its activities, it was decided that certain health problems should have priority within the work of WHO, namely, tuberculosis, venereal disease, malaria, malnutrition, and maternal and child health. The activity of the organization has since expanded considerably. Mental health, for example, has been added to the subjects to be actively supported, and in 1950 a section on social and occupational health was established within the Division of the Organization of Public Health Services.

Occupational Health Problems

The earlier international work on occupational health is important. The main objective of the permanent International Commission on Industrial Medicine, founded in 1905, was the organization of international congresses of which the last two were the Ninth International Congress held in London in 1948, and the Tenth held in Lisbon this year.

The International Labour Office has, since 1920, been working in the field of occupational health, and has been chiefly concerned with accidents and occupational diseases. Its activities have included the organization of international conferences, the issuing of an excellent bibliography of occupational medicine, monographs on special problems of occupational health etc.

It is obvious that the work on social and occupational health by WHO must be closely coordinated with the activity of ILO, and in this connexion, in 1948, the first Assembly of WHO decided to set up a Joint ILO/WHO Experts Committee for Occupational Health. This Committee, which first met in September, 1950, consisted of the following members: Sir Joseph Bhore (India) ; Professor Luigi Carozzi (Switzerland) ; Dr. Leonard Greenburg (U.S.A.) ; Dr. Branko Kesic (Yugoslavia) ; Professor Pierre Mazel (France) ; Dr. E. R. A. Merewether (United Kingdom) ; Dr. Leo Noro (Finland) ; Dr. Ismael Urbandt (Argentina) ; Dr. A. Uytdenhoef (Belgium).

The nomenclature and definition of occupational health varies in different countries. According to a very narrow definition, occupational health deals only with diseases or injuries caused by conditions of work, that is to say occupational diseases and accidents. According to a broader definition, on the other hand, occupational health includes preventive medicine and medical care for the workers and their dependants. This means that occupational health would, in practice, include all medical activities. The Joint ILO/WHO Committee of Experts devoted much time at its first meeting to a discussion of the terminology and definition of occupational health. The Commission proposed that the term " occupational health " (*médicine du travail, medicina del trabajo*) should be used. It was agreed that occupational health should aim at " the promotion and maintenance of the highest degree of physical, mental and social well-being of workers in all occupations ; the prevention amongst workers of diseases caused by their working conditions ; the protection of workers in their employment from risks to health ; the placing and maintenance of the worker in an occupational environment adapted to his physiological and psychological equipment, and, to summarize : the adaptation of work to man, and of each man to his job ". This definition gives a very logical limitation to the field of occupational health which will include all the workers' health problems in relation to their working conditions or their employment. Occupational health will thus not only include occupational diseases and accidents, but the application of preventive medicine to industries or other places of employment confronting problems such as the prevention of tuberculosis and other airborne infections, the promotion of mental health and

prevention of neurosis, the rehabilitation of workers disabled by disease or injury, the placement of workers, routine and special periodic examinations and, finally, health problems affecting special groups such as young persons, women, and, in the western hemisphere, the elderly worker.

A close liaison between WHO and ILO will avoid overlap, and allow each body to follow the other's activities. While WHO followed with interest the ILO's work on accidents and occupational diseases, it would most usefully make studies in other fields of occupational health such as airborne infection, mental health, and geriatrics where it has the necessary experts and experience.

After some preparatory studies by Dr. G. R. Hargreaves, following a request from the Scandinavian countries for information on programmes for mental health in industry, WHO, in 1950, sent Dr. R. F. Tredgold, an English psychiatrist, to spend six weeks in Finland, Sweden, and Norway to study industrial medicine and discuss mental health problems in industry. As a result of this mission, a short course in human relations in industry has, this year, been arranged in England for the benefit of the Scandinavian countries. During this course, these problems were discussed from different points of view by industrial physicians, psychiatrists, psychologists, social workers, industrial managers, and workers, who reported on English, and Scandinavian experiences.

WHO may organize seminars or issue monographs on important problems within the field of occupational health. (It is also important to stress the occupational health point of view at seminars or expert meetings dealing with problems allied to occupational health.) A seminar for sanitary engineers held at The Hague in 1950 was arranged by WHO, the International Health Division of the Rockefeller Foundation, and the Government of the Netherlands. (At this seminar lectures were also given by a physician and an industrial hygiene engineer to inform the members present of basic problems of occupational health.)

The information services such as indexing, abstracting, or reviewing articles by ILO and WHO are already coordinated.

In the future several practical problems within occupational health will be considered by WHO. These problems include the promotion of health in small industries, the arrangement of part-time work for housewives working in industry, and occupational health problems in different climates.

Many practical problems also arise within the United Nations programme for the Technical Assistance for Economic and Social Development of Underdeveloped Countries. As it is useful simultaneously to develop the industries and the industrial health services in a country, it is clear that there are many important occupational health problems connected with this programme.

One of the main obstacles in raising health standards of people is the lack of trained personnel. WHO has supported this training by offering fellowships to different countries. During 1947 to 1950, in the field of occupational health, 13 long-term fellowships have been given to doctors and engineers.

It is thus made clear that occupational health is part of the responsibility of the World Health Organization and will be developed, in cooperation with ILO, as part of the programme of this organization.

Summary

A short survey is given on the general activity of WHO, the specialized agency for health problems of the United Nations. The scope of occupational health is discussed, and a survey of present and future activity of WHO in the field of occupational health is given.

Brit. J. industr. Med., 1951, **8**, 209.

THE BEARING OF EXPERIMENTAL PSYCHOLOGY UPON HUMAN SKILLED PERFORMANCE

BY

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I am going to try to tell a story of interplay between ideas and experiments. The last 15 years have been a period of intense and concentrated activity for all psychologists working in the University of Cambridge. To those of us who have been closely identified with it, the whole development has assumed a character of exciting and engrossing adventure. I believe nobody, at the beginning, could possibly have foreseen to what precise issues our early, and very general, directing ideas would lead us. But as experiment has grown from experiment these ideas have become clarified and defined until we have now, so it seems to me and to many others, an approach and a technique in the controlled study of realistic human behaviour, which are of great significance in many fields, and certainly not least in the vast field of industrial medicine.

The volume and detail of work completed have been very great. If we consider the activities of only one of the Cambridge Units, the Unit for Research in Applied Psychology, established by the Medical Research Council in 1944, we find that up to July of the present year 156 reports, the large majority of which are directly experimental in character, have been circulated. To these must be added a considerable number of published papers, all similarly of a basic experimental character, which were issued by the Nuffield Unit for Research in Ageing, established two years later. Generous support from the Rockefeller Trustees, from all three of the Fighting Services of this country, and from a number of industrial sources, has produced its full share to swell the stream of recorded research. All the time there has been a steady growth of contributions from members of the University staff and from research students who have come to us from many parts of the world.

Since the bulk of this work is experimental, its detailed description has often taken a somewhat technical form. It would be unreasonable to expect any student or investigator, who has not himself been at the centre of operations, to be able, without great labour, to construct a clearly defined idea of what has already been achieved, and of the main growing points of present and future advance.

The time appears to have come for an attempt to present a synthetic view of the whole of this research, and to try to do it in a manner sufficiently free from technicality to render it possible for any interested reader to understand, and, if it seems desirable, to make use of the fundamental ideas which have shaped its development. This, therefore, is what I shall now try to do, and if I adopt a somewhat personal style, it is only because that seems the best way to convey a little of the thrill and feeling that something yet more important may be waiting "just round the corner", a feeling which all of us who have been actively concerned have had and still cherish.

The Beginning

It is always difficult to fix a beginning for any ideas which grow slowly into a new approach to longstanding problems and a new set of techniques for their study. No doubt in this case there was a process of gradually accumulating discontent with the classical methods of the experimental psychologists in a good many different areas of investigation. Visual perception had been dominated by the employment of squares, triangles, circles, and similar figures drawn in two-dimensional form on blank cards, very different in their properties and perceptual demands from the contours, shapes, and meaningful objects of the visual world, and usually with all the vitally important distance and depth

characters lacking. In the early 1930s I myself had reached and published a demonstration that in memory studies great preoccupation with "nonsense" material may become more of a hindrance than a help. When, in the course of the second world war we were forced, for practical reasons, to ascertain how people use their skill, both mental and bodily, to track targets, to drive vehicles, to pilot airplanes, or to control them from the ground in concerted flight, we confronted much the same difficulty. The units used in the classical experiments, (simple thresholds of movement; reaction-times having, often enough, succession, but nothing that could be called an ordered sequence; items in the skill separated from everything else, having the accredited form of "stimulus—response", but devoid of any character of accomplishment of an internally varied task) seemed, if they were forced into the world of everyday work and play, to have the same taint of "nonsense".

One day, fairly early on in the war, I had been out with Kenneth Craik to look at some new anti-aircraft equipment. When we were being driven back to Cambridge we fell into discussion about how to investigate air pilot's fatigue. For some time I had been trying to think how the conventional laboratory procedure for the study of fatigue might be supplemented and perhaps improved. The current methods, based almost wholly upon the investigation of simple and relatively isolated muscular and mental activities, seemed to me so devised that practically only three types of result could be recorded accurately: the amount of overall deterioration of work, the occurrence of checks and spurts in work, and, if the activity were pushed to a certain distance, the final collapse of work. What we needed to know was precisely how skill, in long-continued exercise, may change and perhaps deteriorate. So I asked Kenneth whether he could design and build controls for an experimental cockpit. We should, it seemed to me, try to pick out the "key", or essential, elements in the control behaviour of a pilot flying by instruments. We should record these accurately, if need be for long periods, and also as much as possible of the associated but perhaps less critical activities. Then we should know, not only whether less or more work was being done, but also by what kinds and amounts of change in the co-ordinated control behaviour these, and other, variations, were being brought about.

As anybody who knew him will remember, Craik had a wonderful big black wallet. It was always stuffed to overflowing with odds and ends of bits of paper, with jotted notes in a most illegible handwriting about projected experiments, with dates of engagements seemingly in a terrific muddle, with impromptu drawings of experimental apparatus. Out came this wallet. He found an available bit of blank space. A diagram began to grow.

In a quite definite sense this was the beginning. The very next day Craik was in the laboratory workshop fashioning the experimental controls for what came to be known as "the Cambridge cockpit". The experiments were done later, first by Craik himself, and then, more fully, by G. C. Drew (now Professor of Psychology in the University of Bristol), and by Russell Davis (now Reader in Clinical Psychology in the University of Cambridge).

It is fair to claim that these experiments, more than any others, gave us the guiding principles which we have been able to use, in many applications, with growing definiteness, ever since. They demonstrated that the characteristic changes which take place in skilled human performance with long continued exercise are very different from those which normally mark the continuation by repetition of isolated muscular or mental activity. What made the demonstration possible was that we had refused to break up the skill into bits and pieces, and to be content with a measure of how well the performer could, at any stage, carry out a selected item of his work. We had discarded the view that if we could find out, in terms of time taken, or effort expended, or degree of accuracy achieved, the normal limits of response for each successive move in the skill cycle, we could somehow infer what should be expected in terms of overall time, or effort, or accuracy for the whole cycle. We knew now that in order to discover anything important about skilled performance we must find a way to get right inside the skill itself, and to relate, within the experiment, actual overall measures with actual measures of the ways in which the internal constituents were being carried out.

It also became plain that, certainly in this type of skilled performance, and perhaps in others, not all of the internal constituents are equally important. There are "key" or "master" elements round which all others tend to be grouped, so that if the key activities are properly timed and carried out, all the rest will normally go well without much, if any, voluntary effort. How to discover the "master" constituents was obviously a question of predominant importance.

Moreover we learned that the absolute time (especially the least time) taken to complete any movement, or decision, involved in skilled activity, is of very little significance. What matters is the "spacing" or "timing" of movements, or decisions, or both, in their natural succession. This meant

that " reaction-times ", in the classical sense, could tell us very little, and we began to see why, in spite of the immense amount of work that had been done about them, not much had been learned from them that seems to have a practical or theoretical bearing upon the carrying out of any known skill. This " timing " obviously demanded consideration of the arrangement and interpretation of the perceptual " display ", as well as of the consequent execution of any active movements. The " receptor " elements in skill, much neglected in many forms of motion study, at once assumed most important functions.

Finally an extremely interesting point emerged from these early experiments resting on the difference between what a man can do and what he will do. At every stage of a skilled performance, except at the very beginning, and not always then, two thresholds are measurable : the threshold of ability and the threshold of range, or of indifference. The first is the least perceptible change of display which *can* produce a response ; the second is the range of perceptible change beyond which a response *will* be made. The first can remain constant while the second has altered notably. On the face of it, it seemed that this must bring into our experiments the persistent and little understood condition called " motivation ". But this was not motivation in any ordinary sense, for both to himself and to anybody else the performer could all the time remain as keen as ever. Some pilots, after about two and a half hours of continuous exercise, required instrument changes double or treble the size of those which were effective at the beginning, before they would do anything about them. Yet it was easily demonstrable that their ability threshold had not risen, and they were themselves entirely unaware of any difference in this aspect of their behaviour, and honestly claimed that they were doing as well as ever.

We had now, it appeared, achieved a promising method for experimental development, and we were faced by a number of intriguing but reasonably well defined questions. Obviously we must exploit in all possible ways the study and measurement of skilled performance in as natural a setting as possible, and in the form, not of analysed or broken up bits of the complex activity, but of continued exercise. We must try to find out how, in such continued exercise, " key " elements, or moves, can be identified. We must clear up the implications and conditions of spacing in display, and of timing in control. We must go much further in understanding the vitally important difference between what people can do and what they will do. We must be prepared to defend the view that, certainly for a long time, possibly for always, at various growing points our authority must be the trained judgment, what the medical man might call " diagnostic flair ", and that though interpretations must be given as fully warrantable an experimental basis as possible, the experiments must be designed and developed not only with technical skill but also with psychological wisdom.

Development

In attempting to present a picture of the post-war developments of the experimental psychology of skill in Cambridge, I am bound to select only a few of what I judge to have been crucial points of experimentation and interpretation. In fact every member of the working units and groups concerned has contributed towards whatever success has been won. Those whose work I have selected would be the first to agree that a very different selection might just as well have been made.

Importance of Display.—" Display " is the term which is used for all the environmental signals which the skilled performer uses to guide his work, to initiate and stop the movements or decisions which he has to make. " Control " is the term for the mechanical and electrical devices which have to be used by the performer in the vast majority of everyday skills, and also for the directing functions of decisions and movements themselves. It is clear that a part of the information which the operator is using comes from the display, in the sense just defined, and a part from the proprioceptive impulses set up by his movements. Perhaps there is also some direct effect of the central activity involved in making decisions.

It appears more and more certain that if there is one outstanding characteristic of efficient skilled performance, whether in work or in play, it is the consistent timing of successive steps or moves. We can show, for example, that the highly skilled transport driver tends to maintain a persistent pattern of behaviour, making the necessary adjustments of acceleration, deceleration, gear-changing, change and speed of change of direction, within small limits of difference relative to the overall rate at which he is travelling and to the rate of movement of other relevant items in his visual field. Neither to observation nor in measurement are the particular adjustments made at an enhanced speed. In fact, the skilled performer everywhere usually seems to have " plenty of time ". The great thing is that successive moves flow one into another without check or hurry, without waiting or snatching. What sort of information is it that makes this possible, and does the information act all the time or only intermittently ?

G. C. Grindley and a number of collaborators have carried out a long series of experiments with very simple movements and pressures, by the exertion of which the operator is required to bring a pointer on a visual scale to a given position and stop it or keep it there. Any normal subject can learn this quickly, and provided the visual check is provided, can repeat or maintain the movement or pressure with great success. But as soon as the visual information is removed relatively large errors appear. They are, within limits, haphazard, and the subject himself knows little or nothing about them. With small movements and pressures the errors are predominantly of overshooting, but in whatever direction they start, they are apt to continue up to a limit and then be reversed. It seems as if the "stop" signal must come mainly from the display, and as if the proprioceptive information that is available operates only cumulatively and in an intermittent manner.

Normal skilled adjustments, however, do not consist of single directional movements. The moves form series, with varied change of speed, extent, and direction. Accordingly other investigators have carried out the same pattern of experiments, but with continuous tracking. The critical points are near by where marked changes are required, especially, in this case, changes in the direction of movement. If the display is removed, or made intermittent, the changes will normally be made too soon or too late—far more often too late—with consequent unwanted deceleration or acceleration afterwards.

The skilled operator is not using equally, or in the same manner, all the information that is available to him. In particular for stopping and starting, for deceleration and acceleration, and for their commonly associated changes of direction, display features, appreciated by exteroceptive perception, are of predominant importance, and make possible genuinely graded, as distinct from intermittently cumulative, responses.

Yet it is clear that the proprioceptive information is not being entirely ignored. C. B. Gibbs and others, for example, have shown that for many purposes in which successive positional adjustments are required, a pressure type of control, in which free movement is reduced to a minimum, is easier both to learn and to maintain even when display features are unchanged. And, for reasons at present unknown, this is particularly marked in relaxation phases of control, as contrasted with active contraction phases.

The broad conclusion from all these experiments is that display has a preponderatingly important part to play in all skilled operations at all of their stages. Where the operations are machine controlled, as is now the case with the vast majority of industrial skills, display design is from first to last, a matter of vital importance. Obviously no general discussion can deal with design in detail, though the details have been worked out in many instances. The important characteristics of display signals are: number, location, size, shape, direction and rate of change, and modal variety. In all of these the desirable feature is the greatest possible freedom from ambiguity. That display may possess this marked significance has a number of disturbing implications for many developments of motion study and job analysis.

Anticipation.—Many people, looking at quick-moving industrial operations, must have noticed that the operators seem to be interpreting signals ahead of the action point which they have reached. Yet hardly any investigator has paid much attention to the anticipatory functions which can be easily identified in almost all skilled performance. Innumerable studies and speculations have been made of and about remembering. But nobody until lately has seriously set himself to discover the normal range of anticipation, what it does to the movements and decisions that make up a skill, and through what mechanisms it operates. E. C. Poulton, H. Kay, Miss M. A. Vince, J. Leonard, and others decided to try to fill up the gap.

First they have shown that when display signals succeed one another fairly rapidly, especially in most psychophysical skills when the intervals are rather less than 0·5 sec., the interpreting senses do normally run ahead of their associated actions. This does not usually speed up the movements, but they succeed one another in a more fluent manner, and the resting interval from move to move is reduced, while at the same time the effort of changing, for example from one direction to another, is lessened.

There are at least three different kinds of anticipation. When signals can be treated as coming along in a single related stream, and each signal has its appropriate response, as in many conveyor belt operations, there is straightforward "receptor effector" anticipation. Its temporal limits are small and sharply cut off. It can work one, two, or, exceptionally, three steps ahead of the action point reached. It breaks down badly if the spacing of signals demands a more extended span, and it cannot deal with simultaneous signal streams all of which demand action.

But in many skills, both inside and outside industry, the signals possess an order and are more or less regularly recurrent. It is a character of

human perception, as distinct from direct sensorial response, to be able to appreciate order, arrangement, and design. So the order and recurrence which have been perceived are used to prepare for their next appearance, and signal arrangements which have, in fact, already passed, are, so to speak, able to project action into the near future. Anticipation span is now extended to cover the whole of an order that can be assimilated by perception within whatever limits of time have been imposed by the manner of its presentation. The cost of this is obviously a loss of flexibility, for if anything novel breaks into the prospective signal scheme the skill suffers very seriously. Also there are severe limits to the number of overlapping, or concurrent, signal streams that can be dealt with by this type of anticipatory behaviour.

Suppose, however, that a situation has to be handled which is developing in many different directions at the same time. This is the kind of case that all centralized traffic control must deal with. It also recurs whenever reports are coming in from many different sources and have to be filtered, analysed, and passed on in a form suitable as a basis for quick decisions and action. It involves executive skill operating at a high level over a wide and varied area. Dr. N. H. Mackworth has been able to show that if, in such instances, it is possible, as it often is, to give foreknowledge of when and where critical developments are likely to occur, the normal result is that whatever the precise character of the critical developments may be, when they are reached, they will be dealt with more quickly, with less effort, and with improved accuracy. The exact limits of range of anticipation in this case depend upon the amount and nature of current activity, but the range is certainly vastly extended and flexibility is regained.

There is much yet to be discovered about the fundamental theoretical implications and the mechanism of these types of anticipatory behaviour, but once again it has been demonstrated that the accurate and sustained timing which is paramount in all efficient and economical skill depends both upon the nature, extent, and direction of the movements and decisions involved and upon a planned and adjusted spacing of display signals.

Speed and Load.—It has become more and more plain that the two predominant internal objective conditions of efficient skilled behaviour are speed and load. Both must be defined carefully. Speed is not measured adequately by the popular reaction-time technique. There is the time taken to initiate an action, once the signal has been given ; there is the time taken to complete the action ; there is the " change over ", or resting time, before the next required adjustment can be undertaken. It is certain that the first two have absolute limits, but these are very rarely approached in any conditions normally met with in industry or in everyday life. It is the " change over " time that is rather readily modifiable, and if an overall required speed of performance, combined with special conditions of display and control, either reduces or increases the change over time beyond limits, the whole performance will quickly lose its smooth and regular appearance. There is some evidence that most people are more intolerant to marked increase in change over, or resting time, than marked decrease. If this is really the case, the reasons, which are not yet known, must be of great interest. It is, however, quite certain that overall speeding-up of performance can alter the timing relations of the successive phases of serial response. It seems likely that it does this principally by a forced reduction of change over time, and when this passes a certain limit, the performance becomes ragged and uneven, and if it has to be continued the performer will inevitably suffer from fatigue and strain.

In whatever detailed manner it produces its effects, overall speed must be regarded as an independent condition of skilled performance. Moreover the present evidence is that if the overall speed is increased or decreased beyond the limits that are consistent with smoothly timed succession of response, the adverse effect piles up at a disproportionately rapid rate with every further increase or decrease.

Load depends on the number and arrangement of distinguishable signals, or signal sources, which have to be dealt with simultaneously or in very rapid succession. Load and speed may obviously be made to vary independently or in any desired order of dependence. Mackworth and Conrad have shown that while each produces its characteristic results, they can be readily combined, and then if either of them is increased or decreased, or if both are increased or decreased, beyond tolerable limits, the deterioration of performance that is produced is extremely marked. The common practice, which is to assume that if either is changed by a known proportionate amount, in order to maintain undiminished skill, the other must be changed in the opposite direction by a corresponding proportionate amount, is wrong. Further, load, in the sense of number of signals or signal streams, must be distinguished from load in the sense of arrangement of signals or signal streams. Some of the war-time experiments, based upon bomb aiming guided by signal clusters, showed that " outlier " signals are extremely likely to produce preponderant and

exaggerated effects, and this has been confirmed with an experimental setting simulating machine-minding. But at the same time the outlier signals are the ones most likely to suffer from the opposite error of intermittent or omitted responses in continued exercise.

Ceiling.—Both speed and load are, in a way, characteristics inherent in the skilled performance itself. There are also external conditions, which do not themselves work into the actual behaviour, but can affect it. The most important of these are the attendant environmental conditions : temperature ; humidity ; the objective length of working spell ; the amount of overall bodily activity required ; comfort. It was Mackworth who first demonstrated that these operate, in a normal working group, within fairly well defined and relatively constant " tolerance limits ". Vary them within these limits and there is no significant change in the skill. Vary them even a little beyond the limits and the change is very striking. It seems exceedingly likely that the best way of defining " normality ", whether in an individual or in a working team, in relation to any specified kind of skilled activity, may be in terms of " tolerance limits " ; but more experiments are needed to demonstrate this. Whether there are any regular conditions which can be safely used to extend the ceiling, except for short intervals, is not yet known. The common practice is to offer enhanced rewards ; but it is reasonably certain that this is ineffective except for spurt demands.

Key Moves.—Earlier in this article I said that one of our aims was to try to find out how key elements, or moves, in skilled performance could be identified. *General* master or key features, important in large classes of skilled activities, are not, as a rule, difficult to find. Even if, as often happens, they are, to begin with, reached by intelligent guessing, they can be experimentally tested. In fact all the characteristics of display and control and their exploitation that have been emphasized in this article are key features in the general sense.

In much the same manner it is easy enough to show that in psycho-motor skills the key characters occur predominantly where change of rate and extent, and more than anything else, of direction of movement are required. Active posture, out of which specific movements may flow easily, belongs to the same *general* master feature group. But so far nobody seems to know much about the postural conditions of efficient skill, except in very early stages of psycho-physical development, and in a general sense. There are more than enough opinions, but hardly any well-founded knowledge. The topic waits for the sufficiently informed and ingenious experimenter.

The outstanding character of mental skills is that, compared with the bodily kind, they deal with situations at a distance, and therefore in symbols. But they have the same feature of moving in ordered and interrelated succession to whatever issue forms an accepted terminus.

And it is quite certain that in such moves there are key times and places, and if these can be picked out beforehand, so that the performer is ready to deal with them, all the near-by associated moves become relatively easy, uniform, certain, and fluent. In specific instances it is often possible to demonstrate by experiment such things as how far ahead it is worth while attempting to pick out and indicate these critical times and places, and in detail how, when this is done, the skilled performance becomes smoother, less tiring, and more effective. Mackworth has achieved this for the typical skill of traffic control, and he has shown in what ways and to what degree the whole process depends upon foresight. There is no doubt at all that it can be done in other instances as well. But when we ask how to detect, and especially how to impart this " gift " of identifying crucial times and places prospectively, at present we have no sure answer. This is one of the instances in which we must be willing to fall back upon " diagnostic flair ".

It must be admitted that the same is true of *particular* key elements and combinations in a very large number of the skilled activities of daily life, especially when, as in most sports and games, the display has to be selected from a freely varying external environment by the performer himself. The *general* key features may tell us where to search, but variations of body build and mental endowment and acquisitions go heavily against the assumption of the single master-key.

Incentive and Motivation.—Motive is anything belonging to the performer himself which puts and keeps his specific skill processes in action. Incentive is anything coming to the performer from outside which sets some motive at work. The level and the persistency of skill depend on them both.

Little is known about either, and, as usual, the less is known the more seems to be asserted in speech and in writing. By far the commonest incentives used are a large variety of rewards and punishments. We know that the former are usually, except in special cases, more effective than the latter. We know something about the conditions under which the latter are of use. We know also that incentive, coming from the outside, operates with severe temporal limits, and can be

held to something like a constant effect only by periodic increase. We know that whenever skilled work or play is being exercised at near tolerance limits, incentive will, and can, do nothing except in a short-lived spurt. Near the beginning of all of our work, Craik, pondering over operations of self-regulating machines, such as the velodyne motor, began to wonder whether it might be useful to think of motive as a kind of feed-back, operating from within a skill and currently with its unfolding, and acting as a kind of centrally appreciated standard, marking any difference between actual achievement and whatever it is the organism is set to achieve. And indeed this has proved to be a fruitful notion, directing many experiments ; and as I have indicated earlier, we have gone some way along this line, learning a little about the priorities and effectiveness of information given either intermittently, in a form of " knowledge of results ", or currently, with practice of a skilled performance itself, through associated internal peripheral and central changes. But it is all the merest beginning, and in any case it cannot be the whole story. The real puzzle lies not in the relationship of performance and " set ", but in what settles and maintains the " set " itself.

The Application of Experimental Techniques to Problems of Ageing

When the Cambridge Nuffield Unit for Research into Problems of Ageing was formed, much of our early work on the measurement of skill had already been completed. There was at that time an imposing array of experimental work on the characteristic deteriorations of reaction which accompany increasing age. Nearly all of it was based upon studies of isolated responses ; reaction-times ; acuity thresholds of many kinds ; steadiness tests ; intelligence tests of the unit item variety ; problem solving ; and the like. Where spells of working activity were studied, little attempt had been made to use any other measures except those of overall performance : amount produced, total errors, total times taken, amount of effort expended, and so on. The general picture obtained was one of small and negligible deterioration at relatively early age, followed sometimes by recovery and sometimes by slight persistent decline, and finally, at advanced age, very often a catastrophic fall.

It seemed to us that the time had come to approach the whole subject in a different manner. Because we knew most about these we resolved first to study the relatively light skilled operations which in fact, owing mainly to improved instrumental and machine technology in all directions, are coming to play a more and more dominant part in organized industry. Our skills must be allowed to keep their natural order of expression, and our measures must go inside the skills. We must give the operative conditions of design in display and timing in control, of speed, load, and ceiling, our primary attention. We must not be too much hunted by the notion of deterioration of skill alone, and supposing that we did find that there are changes in the manner of skilled performance which are characteristic of broad age ranges, we must find out whether these have important implications in regard to the most economical learning of skill at different ages, and its continued, day to day exercise.

The programme was large and undeniably ambitious, but Mr. A. T. Welford and his associates have already shown beyond question that its broad guiding ideas are fruitful and practicable.

First there are a number of technical and technological points of method connected with measuring skilled work from the inside, and with relating whatever goes on inside the skill with a measure of what is produced, or with an overall performance score. Even when we have demonstrated that the measures that we most need are related measures of timing in control and spacing in display, if we are to remain loyal to our view that these must be sought within the natural skill sequence, and not once only, but in continued exercise, any ordinary methods of recording and evaluating are excessively difficult and time consuming. Welford has, however, been able to develop an electronic time-and-error recording device which gives us the critical scores we need in such a form that they can be fed into automatic computing machines to give us speedily whatever statistical analysis is desired. There seems every prospect that this method of recording and evaluation can be greatly extended, and that it will open up fields of investigation which have so far been too difficult to explore in any detail.

The general story is consistent with most of what has been said already. Laboratory and field studies alike show that, as age increases, it is the timing of control responses that suffers most. The difficulty begins to appear early, in the late twenties and early thirties, but except under severe speed and load stresses, it is usually countered by a more " canny " use of the display signals, especially, probably, by a more deliberate and effective, though usually unwitting, extension of anticipation, and often by some reduction in a number of movements and decisions. Consequently overall performance does not suffer, and may even go on improving, unless there are rather drastic changes in the general design of the methods and environmental conditions of the performance. The bother is that nowadays very rapid improvements in machine design make

such drastic changes common, and unless these are introduced with care and wisdom, serious difficulties are likely to develop, especially in the age range from about 40 to about 60.

The evidence also shows that the increased intolerance to speed which accompanies ageing is not, during the period of a normal working life, or even rather longer, due to any natural increase in the time taken to initiate a response, or to the movement time itself, but to irregularities of change-over time, particularly, probably, in rather long spells of continued activity. Field studies appear to show that the trouble is most acute when skilled movements have to be combined with a large amount of general bodily activity, and both the movements and the general activity have to be carried out under imposed speed stress.

What causes the greatest difficulty of all is dealing with novel clusters of signals, and especially from the forties onwards the skilled operator cannot reasonably be expected to make the necessary re-adjustments quickly and automatically. Whether a little judicious retraining could maintain the required level of performance is not yet certain. Very likely it could, but the method of training must certainly be adapted to the age-range of the performer. In a broad sense it seems to be coming out more and more that display and load assume greater importance as age increases.

Any attempt to explain the precise mechanism of all this is at present bound to be pretty much of a guess. But it seems not unlikely that as what is called " middle age " approaches, there is a tendency to make more and more exclusive use of the second of the three main types of anticipation. The appreciation of order and pattern in events requires certainly an alert intelligence. But it can, though of course it need not, avoid the added burden of a recurrent or continuously active selective observation. The anticipatory function in rapid skilled performance cannot be avoided, for without it the essential smooth quality of skill will be lost. It may be that there is normally some retraction of span or range of direct exploratory anticipation, and with it some extension of span of the kind that rests upon short or long-term storage or recall. There is then inevitable loss of flexibility.

In spite of all of this, skill prognosis for age becomes steadily more and not less favourable as we come to understand better the nature of the changes that take place. Given a due regard to essential psychological conditions, a normally healthy population should be able to maintain and modify acquired skills, and even achieve new ones, well beyond any age that is now considered to mark the term of an active working life.

We began all our work on ageing in the laboratory. This was partly because we were proposing to develop new methods of assessment, and partly because we knew that when we went out into the industrial field we must be equipped with at least some guiding ideas of what to look for. Without these, observation of the field type gets bogged in a mass of varied detail. But observation alone, and even observation and field experiment cannot carry us all the way when we are concerned with direct industrial problems. We must have records, especially when types of training and learning about which practically nothing is known come up for consideration, as they obviously do in this case. We have found that reliable and relevant industrial records bearing upon the problems which have been indicated are very rare indeed. It is a matter of great urgency that this gap should be filled.

The Study of Human Skill, Performance, and Industrial Medicine

No doubt it is right and natural that industrial medicine should still be greatly preoccupied with detailed studies of specific hazards which must be encountered in particular industries, groups of industries, and industrial operations ; and with problems concerning the treatment of the worker who falls a victim to these hazards, and how they may be prevented or the workers adequately safeguarded. Toxicological problems, a large variety of types of specific industrial diseases and acquired disabilities of bodily function, the treatment and prevention of burns and other injuries—these and many other questions of the kind that everybody at once recognizes to be " straight medical ", must remain in the forefront of the industrial medical officer's attention.

Yet nobody can now ignore the facts that modern large scale and highly organized industry has to face up to a lot of human problems, the criteria for the occurrence and severity of which are limited efficiency, the piling up of unwanted and avoidable fatigue and strain ; an accumulation of errors leading to accidents that could just as well never occur at all ; irregular working habits, and the growth of simmering or open dissatisfaction often leading to dispute, the real causation of which is frequently misunderstood. For the most part these maladjustments do not issue in any definite or identifiable bodily disease, but in extreme cases, which are nevertheless sufficiently common to lead to plenty of trouble, they do produce a crop of nervous and mental disorders.

In all these instances the basic conditions are exactly the same as those which produce the prob-

lems which are generally regarded as a proper concern of an industrial medical service. The body and the mind are set to work under circumstances with which they cannot deal without impairment of the activity that is demanded. It is the medical habit of mind, of learning to identify early symptoms of such impairment, and then probing beneath the surface to find out their real causation, that is most of all needed. It should never be forgotten, though it often is, that the body that was responsible for nearly all the pioneer work in this country on the scientific investigation of the matters which I have been discussing, and for the great bulk of its subsequent development, was the Medical Research Council through its Industrial Health Research Board : and that very nearly all the other organizations which have played a great part in the same field during the last 15 years or so have also had extremely strong medical interests.

It has been one of my chief aims, in writing this article, to show that the study of skill in industry, and the general and specific conditions alike of its impairment and of its healthy exercise, has become as technical as that of any of the widely recognized industrial diseases and hazards. The time has come, I would maintain, when every progressive industrial medical service must have its own group of professionally qualified investigators well trained in the principles and practice of experimental psychology. Their relation to the practising industrial medical officer should be exactly that of the toxicologist, or of the specialist in chest or heart diseases. The doctor in the industrial field must know what to look for, what records he, more than anybody else in industry, is in a position to appreciate and can be relied upon to collect systematically and in a sensible form. Now that we are certain that skill can and must be studied in its natural setting of sequential exercise, now that we know something about the key features of its efficient practice, there is a vast amount of valuable information and original observation which can be collected and carried out without any elaborate instrumentation.

I should be the last person to maintain that the approach which I have here attempted to describe, is the only one that should be tried. By all means let influential people go on seeing what they can do by repeated exhortation. Give all possible chances to every wise development of the " science of human relations ". But unless, also, the conditions affecting the healthy and productive exercise of skill are studied scientifically and secured in practice, any number of appeals, any amount of " understanding " management, and the most expensive development of external incentives and amenities in the factory, will not heal troubled bodies, troubled minds, and a troubled society.

Brit. J. industr. Med., 1951, **8**, 218.

THE EFFECTS OF BAL ON THE METABOLISM OF LEAD AND ON THE SYMPTOMATOLOGY IN LEAD INTOXICATION*

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The effects of injection of BAL on the metabolism of lead has been studied by Eagle (1948) and by Ginsburg and Weatherall (1948) in animals poisoned with lead acetate, and by Ryder, Cholak, and Kehoe (1947) in human cases of acute lead poisoning.

The action of BAL has been shown to be the same both in experimental animals and in man; in animals it had no demonstrably protective action, and on occasion appeared to accelerate the toxic effects of lead acetate in rabbits; similarly in man, three days' treatment with 1·7 g. of BAL was without beneficial effect. Characteristic effects were observed on the metabolism of lead, inasmuch as there followed a rapid drop in the lead concentration in the red blood cells, and an immediate rise in urinary lead concentration, to a degree far greater than that observed from any other kind of treatment. The plasma and faecal lead concentration were unchanged by BAL treatment.

Eagle (1948) advised caution in the use of BAL, although he did not see evidence in man of toxic effects in cases of lead poisoning. He recommended four-hourly injections of 2·5 mg. per kg. body weight repeated four times a day and continued for two to four days, diminishing thereafter gradually to about two injections a day.

Ginsburg and Weatherall (1948) used the Th. β isotope of lead to study lead acetate distribution in tissues. Administration of lead acetate was followed by 50 mg. per kg. BAL up to 23 hours later. This resulted in increased urinary excretion of lead and a shift in the tissue distribution from the liver, the spleen, the red cells, and the bone marrow to the skeletal and cardiac muscle.

Our studies on BAL treatment in human cases of lead intoxication were started two years before reading Eagle's report. The first results of our studies were referred to by Angeleri (1949) and later at the International Meeting on Industrial Medicine held in Milan in June, 1950 (Vigliani, Zurlo, Angeleri, Meschia, and Sartorelli, 1951). In this communication we shall report on those early results and also on more recent results obtained since June, 1950.

Results

Twenty-seven patients (25 men and two women) with occupational lead poisoning have been treated with BAL; fourteen of these were suffering from acute lead colic on their admission to hospital, and the others had had lead colic some few days or weeks before. The doses of BAL used were generally low; in no case was more than 450 mg. injected on any day; in a few cases the dose was 50 to 100 mg. a day. Such low doses were held to be necessary on account of the adverse disturbances to which BAL gives rise in lead colic, and to which we shall refer later. In 14 of the patients blood and urine lead were studied using the dithizone method; in three cases the method was applied to the bile and the gastric juice.

In most cases the excretion of urinary coproporphyrin was studied both immediately before and at periods after the injection of BAL, either from day to day for a few days or, in some cases, for weeks.

Lead in Blood.—The average value of lead in the blood of our patients taken in the morning before breakfast and before any treatment with BAL was 122 μg.%. (In the cases with active colic the average value was 138 μg.% and in that of the remainder 116 μg.%.)

Injection of 2 to 5 mg. per kg. BAL brought about a marked reduction of the lead in the blood, this effect being reached a few minutes after the injection and attaining its greatest intensity some

* Rendered into English by Dr. M. W. Goldblatt.

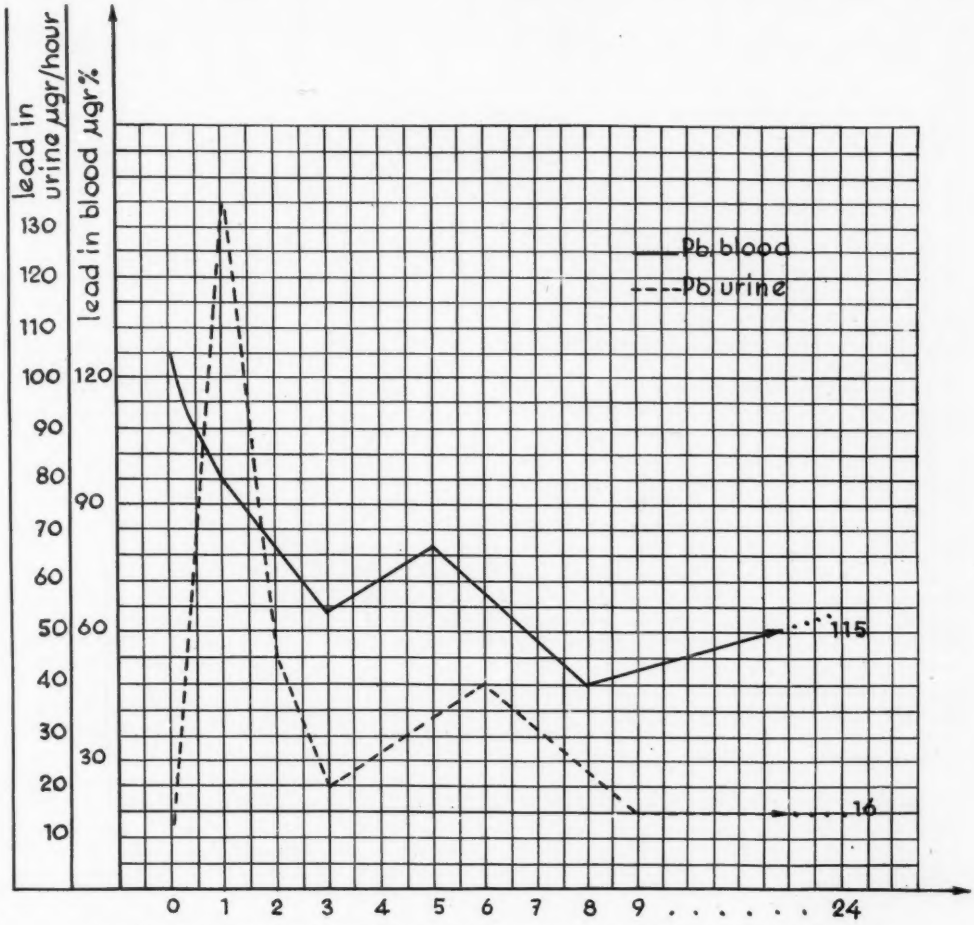

FIG. 1.—Behaviour of lead in blood and urine following an injection of 2–5 mg./kg. BAL (mean of 10 cases).

eight to 10 hours later. This fall was very often interrupted between the third and the eighth hour by a sudden increase, sometimes slight, sometimes quite considerable. Twenty-four hours after the injection, the lead in the blood had risen to 80 to 90% of its level before the injection (Fig. 1). One patient received 50 mg. BAL on one day, and 150 mg. two days later; the degree of reduction of the blood lead level was the same on both occasions.

A series of one to three injections per day of BAL for several days in doses varying from 2 to 7 mg. per kg. daily caused a progressive reduction in the lead content of the blood, sometimes sufficient to reduce it to 30% of the value before treatment. Cessation of treatment with BAL was followed by a rise until the lead content returned in a few days to the level before treatment (Fig. 2).

In two cases the lead content was determined separately in the clot and in the serum before and two hours after injection of BAL. No change in the serum lead was detected.

Lead in Urine.—In our cases the average excretion of lead in the urine before treatment with BAL was 12·6 µg. per hour; in the cases of active colic it

was 14·6 μg. per hour and in the remainder 11·2 μg. per hour.

A single injection of BAL, even a dose of 50 mg., caused the lead to increase markedly in the first hour, reaching a level six to 25 times (average 13·3 times) greater than the average hourly excretion before the injection. In the second hour the lead excretion was still two to nine times (average four) greater than the pre-injection level. The level then rapidly diminished, although it remained higher than the pre-injection value throughout the day. In the 24 hours following treatment with BAL the lead eliminated in the urine was on the average 2·6 times higher than in the 24 hours prior to it (Fig. 1). The major portion of the lead excreted in the 24 hours following the injection of BAL was eliminated in the first three hours.

It will be seen that the amount of lead excreted in the urine is not proportional to the level of lead in the blood ; there is considerable variation in the capacity of different subjects to excrete lead in the urine. It follows, therefore, that the ratio between the 24 hour urinary lead and the blood lead concentration is not constant from one individual to another.

In our cases the increase in lead excretion brought about by BAL was not so much related to the quantity of BAL injected as to the pre-injection ratio between the 24-hour urinary lead excreted and the concentration of lead in the blood : the higher this ratio was, the greater was the increase in the excretion of lead brought about by BAL. In other words the effect of BAL on urinary lead was greater in those cases in which there was already a high urinary lead excretion in relation to the quantity of lead in the blood (Table 1).

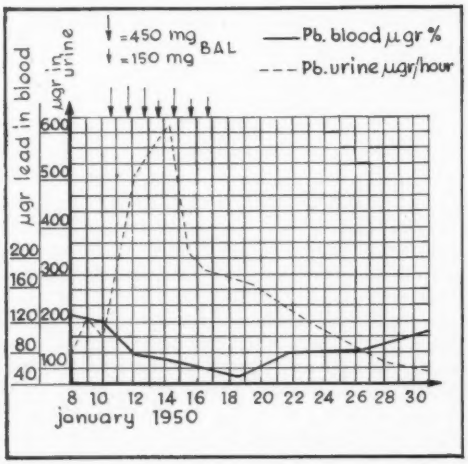

FIG. 2.—Effect of treatment with BAL on blood and urine.

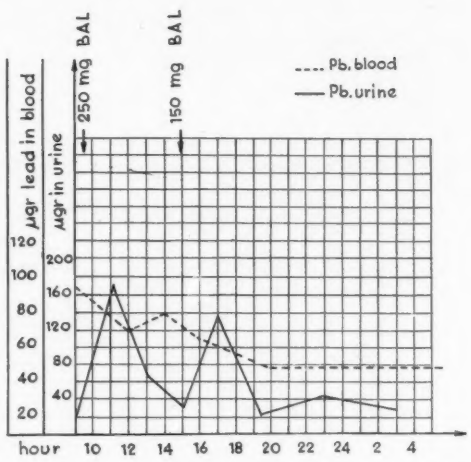

FIG. 3.—Effect of two injections of BAL on blood and urine lead level.

Taking the total mass of blood to be about 8% of the weight of the body the quantity of lead which disappeared from the blood three hours after an injection of BAL of 2 to 3 mg. per kg. can be readily calculated. In our cases this quantity was on the average 2·1 mg. (maximum 3·4 mg., minimum 1·2 mg.), whilst the quantity of lead eliminated in the urine in the same period was on the average 0·4 mg. ; maximum 0·8 mg., minimum 0·1 mg. (Table 2).

It thus is apparent that only a small part (about 1/5) of the lead which leaves the blood after giving BAL passes over into the urine, the greater part is carried over into the tissues, probably mainly into the skeleton (Ginsburg and Weatherall, 1948). Three or four hours after the cessation of the action of BAL the lead which had passed into the tissues returns to the blood, bringing about the observed increase of blood lead which can be seen between the fourth and the eighth hour after the injection. This effect is seen to be greater in those cases in which the urinary excretion of lead was high in relation to the blood lead concentration and in which the elimination of lead had been found to be high in the urine as a result of BAL. If in a patient who had received an injection of BAL of 2 to 4 mg. per kg., then a second injection of BAL is given more than three hours later or one or more days later, the same variations in blood and urine lead are seen as were produced by the first injection (Fig. 3). But if the injections are continued their effect becomes progressively less.

TABLE 1

INCREASE IN EXCRETION OF URINARY LEAD AFTER INJECTION WITH BAL

Case No.	Name	Before Injection of BAL		Ratio 2/1	BAL Injected (mg.)	After Injection of BAL	
		(μg. Pb per 100 ml. blood) 1	(μg. Pb in 24-hour urine) 2			(μg. Pb in 24-hour urine) 3	Ratio 3/2
1	P. Ang.	260	216	0·8	200	431	2·0
2	T. Mar.	134	150	1·1	200	408	2·7
3	R. Nat.	122	160	1·3	2 × 150	326	2·0
4	B. Pie.	88	124	1·4	100	303	2·4
5	M. Lue.	165	309	1·8	3 × 100	440	1·4
6	C. Ado.	138	280	2·0	150	584	2·1
7	D. Pao.	110	225	2·0	150	650	2·9
8	B. Car.	136	280	2·0	50	440	1·6
9	B. Mar.	107	247	2·2	2 × 120	1129	4·6
10	D. Dad.	36	98	2·7	150	216	2·2
11	V. Con.	130	482	3·7	200	2376	4·9
12	R. Mar.	98	400	4·1	400	1150	2·9
13	G. Pao.	120	588	4·9	300	3167	5·4

TABLE 2

TOTAL AMOUNT OF LEAD LOST FROM THE BLOOD AND THE URINARY LEAD OUTPUT AFTER BAL INJECTION

Case No.	Name	Weight (kg.)	Pb per 100 ml. Blood (μg.)			Pb (μg.) Lost from Total Amount of Blood (8% body weight)	Pb Eliminated in Urine in First 3 Hours after BAL (μg.)	Urinary Pb as Percentage of Pb Lost from Total Blood
			Before BAL	3 Hours after BAL	Absolute Fall			
1	C. Ado.	63	138	71	67	3377	264	7·8
2	B. Pie.	61	88	48	40	1952	99	5·1
3	B. Mar.	53	108	69	39	1654	137	8·2
4	R. Mar.	57	98	70	28	1277	525	41·1
5	G. Pao.	64	120	62	58	2969	810	27·3
6	B. Enr.	60	100	75	25	1200	386	32·2

A series of one to three injections of BAL daily for several days in doses of 50 to 450 mg. a day brought about an increase in urinary lead for the first three to five days, followed by a reduction to the pre-treatment levels. Parallel with this effect the blood level fell to 30 or 40% of the original level. Cessation of the administration of BAL produced a tendency in the blood and urinary lead to return in a few days to approximately initial levels (Fig. 2).

A second course of injections brought about a new rise in the elimination of lead in the urine, and a fall in blood concentrations ; the effect, however, was much less marked than that brought about by the first series. Doses of 250 to 450 mg. BAL a day had a greater and more prolonged effect than small doses of 50 to 150 mg. per day. In the latter

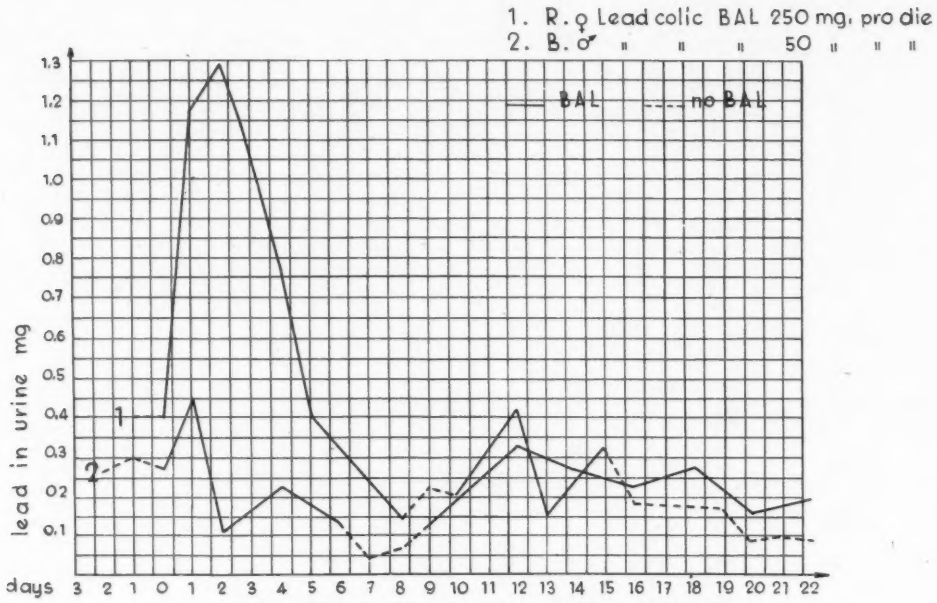

FIG. 4.—Effects of two consecutive treatments with BAL on urinary lead.

cases the rise in urinary lead lasted only two or three days, even when the BAL administration was continued for a considerable period (Fig. 4).

Lead in Bile and Gastric Juice.—Lead was determined in the bile and gastric juice in order to discover whether BAL caused a rise in lead excreted by the liver and stomach mucosa as had been found for the kidneys. This seemed probable inasmuch as it has been known for a considerable time that lead is secreted into the bile and gastric juice.

The test was carried out by introducing a gastric tube into the stomach or duodenum according to the fluid to be collected. After 30 minutes' control period BAL was injected in doses of 2 to 3 mg. per kg., the bile and gastric juice being collected for one to three hours. The lead determination was carried out on the bile, collected every 30 minutes, and on the gastric juice aspirated every 15 minutes.

Lead in Bile.—No significant changes were observed in the quantity of lead excreted in the bile of three patients who were recovering from lead colic following the injection of 2 mg. per kg. of BAL. In the hour following the injection the bile contained an increased concentration of lead, but as the volume issuing from the tube was small, the total excretion of bile remained almost unchanged. In the second hour there was neither change in lead concentration in the bile nor in the total quantity obtained. It must be concluded that, in contradistinction to what was found in the urine, BAL exercised little influence on the elimination of lead in the bile, at least during the first two hours after its administration.

Lead in Gastric Juice.—The elimination of lead in the gastric juice was studied in all cases after stimulation with an injection of histamine. Control observations were made in two patients convalescing from lead colic using histamine alone and without injections of BAL. In one of these a slight rise in tne elimination of lead was observed between the first and second hours after the tube had been introduced into the stomach ; in the other case the reverse phenomenon occurred. On the other hand, in three patients convalescing from lead colic in whom BAL had been injected during the removal of gastric juice, there was found a fall in the quantity of lead eliminated in this fluid running roughly parallel with the fall in the blood lead concentration.

Clinical Effects.—BAL treatment (4 to 14 mg. per kg. per day) carried out in the course of lead colic sometimes caused an aggravation of symptoms. In one patient the effect of two injections of 2 mg. per kg. separated by a period of seven hours was dramatic. After the second injection and whilst

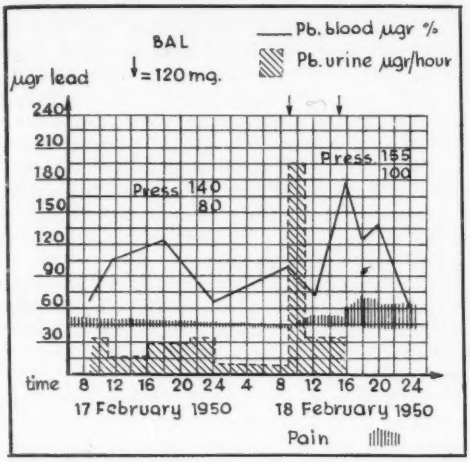

FIG. 5.—Chart of attack of lead encephalopathy following two injections of BAL.

the blood lead concentration was rapidly falling, there arose violent abdominal pain, hypertension, anuria for 16 hours, and an attack of acute encephalopathy (confusion state and severe psychomotor disturbance) lasting two to three days (Fig. 5). In other cases the treatment was tolerated without any adverse effect.

Treatment with BAL in the same dosage when the colic had already disappeared for some days brought about in a few cases a recurrence of abdominal pain, hypertension, and oliguria. Reduction of the dose of BAL to 3 mg. per kg. or less per day prevented such recurrences. Such treatment in cases of lead intoxication in which the lead colic had disappeared for more than two weeks did not provoke any reappearance of symptoms. In some patients there was a strong impression of an improvement of the general condition, and especially of the appetite, body weight, and anaemia, in contrast to the picture presented by untreated patients.

The amount of urinary coproporphyrin during BAL treatment roughly followed the urinary lead. Thus a series of BAL injections brought about a marked reduction in urinary porphyrin after an initial rise.

Discussion

The numerous determinations of lead in blood and urine which have been carried out in our cases of lead poisoning and the marked changes in the distribution of lead in the organism which have been brought about by injections of BAL and which sometimes were followed by aggravation of symptoms, seem to justify certain views on the aetiology and pathogenesis of some of the symptoms of lead poisoning.

There is no doubt that BAL exercises a rapid and intense action on the metabolism of lead. Our observations indicate that BAL combines rapidly with part of the lead contained in the red cells, forming a compound which can be stored in certain tissues and which is only in part eliminated via the kidneys, not at all, or only insignificantly, with the bile, and only slightly in the gastric juice. It is probable that this compound is not excreted at all through the digestive tract; indeed, Eagle (1948) could not detect any increase of lead in faeces after injection of BAL. After the cessation of BAL action lead returns from the tissues to the blood, thus re-establishing a situation almost identical with that prior to the injection.

With a series of injections of BAL for several days the displacement of lead from the blood into the tissues occurs more intensely and lasts longer, because there is no opportunity to return to pre-injection levels between one injection and the next. In some sense, therefore, BAL produces a cumulative effect. Harmful effects attributable to BAL are usually encountered after several days of administration of quantities greater than 300 mg. per day, but only exceptionally after one or two injections. It has been maintained that only lead circulating in the blood is harmful (Schmidt and Weyrauch, 1933) whereas that deposited in the organs or in the tissues has no effect. This statement, however, is not borne out by the fact that the blood lead concentration bears no consistent relation to the appearance or severity of clinical signs and symptoms. It has therefore been suggested (Blumberg and Scott, 1935; Smith, Rathmell, and Marcil, 1938; Wexler and Sobel, 1935) that the clinical symptoms of lead poisoning are more directly related to the lead in the serum or plasma than to that in the whole blood. Our experiments and those of Lauer (1948) have shown that following the injection of BAL no change is found in plasma or serum lead, even when the BAL is re-evoking or aggravating a case of lead colic.

In several of our cases it was observed most clearly that the symptoms of colic appeared, or were aggravated, after the injection of BAL at a time when the quantity of lead in the blood was in fact diminishing. This suggests that it is not lead in the circulating red cells, or that dissolved in the plasma, which is harmful, but rather the lead which has rapidly shifted from the blood to the tissues, or even from one tissue to another, and that it accumulates in a short time and to an excessive degree in some organ or tissue which is particularly sensitive to its

toxicological action. In our case of acute encephalopathy brought about by BAL, about 8 mg. of lead were transferred in four hours from the blood to the tissues, whilst additional lead migrated from one tissue to another (Ginsburg and Weatherall, 1948). It is possible that this notable transfer of lead may have caused its accumulation in the central nervous system, hence the appearance of encephalopathy. Indeed the largest oscillations of blood lead concentrations obtained by us following the injection of BAL were observed in this patient. The aggravation or the re-appearance of colic appears to be due to the migration of lead caused by BAL into elements of the nervous system, the stimulation of which provokes intestinal spasm and the other manifestations of colic. It may be that the intestine is not the tissue involved, for Eagle (1948) did not see any increase in the elimination of faecal lead after the injection of BAL, and we were not able to show any increase of secretion of lead across the gastric mucosa. Our observations tend to support the hypothesis that colic is caused by the alterations in the autonomic system.

Failure to demonstrate the excretion of lead in the bile after injections of BAL is a natural consequence of the transference of lead from the liver to other tissues as observed by Ginsburg and Weatherall (1948); similarly the fall in urinary coproporphyrin can be related to the diminution of lead in the bone marrow, also observed by Ginsburg and Weatherall (1948), and to the general view that coproporphyrins are formed as a result of a modification in the process of haemoglobin synthesis.

There has been much discussion on the usefulness of the process of de-leading. According to Aub, Fairhall, Minot, and Reznikoff (1926) de-leading means the mobilization of lead from the bones with an increase in its elimination. Kehoe and Thamann (1929) advise against any method resulting in rapid liberation of lead from the tissue deposits because such rapid elimination may be followed by the deposition of lead in the central nervous system. The danger of BAL treatment in lead poisoning has been attributed, indeed, to its powerful de-leading effect.

The principal effect of BAL does not consist in a de-leading effect, as ordinarily defined, but in a translocation of lead from the blood and certain organs to other organs. This is borne out by the observed fact that the effect of BAL is to bring about the fall of lead in the blood rather than an increase; the latter could logically have been expected if BAL simply mobilized the lead from the deposits in bone.

Further, the investigations of Ginsburg and Weatherall (1948) have shown that the effect of BAL is to bring about a transference of lead from the liver, the blood, and the spleen to the skeleton.

Having regard to the great changes in the distribution of lead in the organism brought about by BAL, its effect upon the elimination of lead is relatively small. As a result of this shift in the lead, it accumulates in other organs, including the nervous system, in which it may, or could, produce damaging effects. The favourable effect of inducing a large elimination of urinary lead is thereby overcome by the unfavourable effect of an excessive translocation of lead within the organism.

If it were possible to find a remedy which would bring about only de-leading without any excessive shift in the tissue distribution of lead, it would probably constitute the best possible treatment of lead poisoning.

The final impression is that treatment with BAL is dangerous, and especially so in patients suffering from colic or other manifestations of acute lead poisoning; in such cases the medicament should be used with great precaution and in small doses.

Further, we are of opinion that treatment with BAL continued for several consecutive days with two or more injections per day is less effective in eliminating lead and perhaps more dangerous than intermittent treatment, consisting of short cycles of one or two days separated one from the other by two or three days without BAL. The rationale of this scheme of treatment is not to lower the content of lead in the blood, but rather to eliminate as much lead as possible in the urine without at the same time too greatly altering the distribution of lead in the blood and in the tissues.

The fact that in certain cases BAL has caused toxic effects does not mean that it should be completely abandoned as a treatment for lead poisoning; a final judgment is not yet possible until trials are carried out using BAL in small doses and for short periods in chronic lead intoxication.

Summary

Twenty-seven patients suffering from industrial lead intoxication were treated with injections of BAL. Fourteen of these were in a state of colic on their admission to hospital; the others had overcome the colic a few days or a few weeks earlier. The metabolism of lead was studied after a single injection of BAL in doses of 1 to 4 mg. per kg., and in the course of treatment lasting for several days with daily doses of 1 to 7 mg. per kg.

Following the injection of BAL a rapid fall in the blood lead level occurred which reached minimal values eight to 10 hours after the injection, and there was a great increase in urinary lead which reached its maximum one to two hours after the

injection. Where a series of injections was given the blood lead level fell and urinary lead increased for the first few days ; but in the following days the effect of BAL became progressively less. After cessation of the administration of BAL the blood and urinary lead both tended to return to the initial values. A single injection of BAL has no evident effect on lead in the bile, but appears to bring about a diminution of lead eliminated in the gastric juice.

BAL has shown itself to be a rather dangerous medicament in lead poisoning ; its administration during lead colic may aggravate the abdominal symptoms and make them re-appear, even after they had disappeared for several days. In one case of colic two injections of BAL separated by a seven-hour interval brought about an attack of acute encephalopathy. If, after the cessation of symptoms of colic for a week, BAL is administered in doses not greater than 4 mg. per kg. per day, it is usually well tolerated and may perhaps accelerate the process of cure.

The principal pharmacological effect of BAL consists in a transposition of lead within the organism, from the blood and certain tissues towards other tissues, among which the nervous tissue must be considered. The value of the de-leading effect of BAL is relatively small when the unfavourable effects due to disturbance in the internal distribution of lead are considered.

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SOME OBSERVATIONS ON THE TOXIC PROPERTIES OF 3:5-DINITRO-ORTHO-CRESOL

BY

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This paper records experimental work with animals on the toxicity and mode of action of dinitro-ortho-cresol (DNOC or DNC), a compound widely used in agriculture, and occasionally responsible for the death of men handling it in the field.

Most of the data on the toxicity of the related compound dinitro-phenol (DNP) was published in the decade after the 1914–18 war. During that war DNP had been manufactured in large quantities, and many cases of poisoning had occurred among the munition workers who handled it. Both DNOC and DNP were widely used for a few years as "slimming agents". A number of deaths, as well as many cases of cataract, followed the use of these drugs for this purpose. This earlier work on the toxic properties of DNP and DNOC has been fully reviewed by Magne, Mayer, and Plantefol (1932), by Tainter and Cutting (1933), and by Heymans and Casier (1935). More recently, Ambrose (1942) has published some observations on the toxicity of DNOC, including the effects of repeated injections and the cutaneous application of the drug.

In recent times the use of DNOC in agriculture has been greatly extended. Weak solutions (0·01%) are used as ovicides for insect pests and applied as "winter washes" to fruit trees. No casualties of any kind have been reported from among the thousands of people who have used DNOC in this way. Stronger solutions containing up to 20% DNOC have also been used as insecticides and sprayed from aircraft to destroy locusts (Gunn, 1948). Solutions of DNOC (0·5%) are also used as selective herbicides. Such solutions are applied in the early summer to young cereal crops to check weeds. In many cases the solutions have been applied for individual farmers by firms of contract sprayers, among the employees of these firms a number of deaths have occurred within recent years (Hunter, 1950).

The deaths amongst agricultural workers have shown that there are a number of problems to be solved. These accidental deaths often occurred with dramatic suddenness among men who had been handling the material for a considerable time. The possibility of cumulative action of DNOC, the value of estimations of blood levels of DNOC in diagnosis and prognosis, and the effect of environmental factors, such as a high external temperature, nutritional state, and alcohol consumption required investigation. In this paper these aspects of DNOC poisoning are examined. The distribution of DNOC in blood and tissues of poisoned animals was observed, and an attempt was made to explain the experimental findings in terms of modern biochemistry.

Methods and Materials

Estimation of DNOC.—Amounts of DNOC down to 2μg per g. of tissue or ml. of blood or urine could be recovered and estimated by a simple method of extraction in ethyl-methyl ketone and comparison with standard solutions of DNOC in the same solvent. The method is described in detail elsewhere (Parker, 1949). This method estimates both the free DNOC, and that bound to blood or tissue protein.

Certain tissues, such as the liver and kidney, contain an enzyme that will reduce DNOC so care must be taken to homogenize these tissues under conditions where this enzyme will not be active. Initially, the tissues were homogenized in dilute caustic soda, but when more was known about the properties of this enzyme, it was found that homogenization in 5×10^{-3} M. cyanide was a satisfactory procedure for inhibiting the activity of the enzyme.

Detection of Products of Metabolism.—The Derrien test was performed in the way described by Magne and others (1932). Ethereal sulphates were estimated by the method of Senior (1947), and glucuronides by that of Hanson, Mills, and Williams (1944).

The animals were kept in metabolism cages, and 24-hour specimens of urine collected under toluene were used for these tests.

Animals.—Albino rats from the Ministry of Supply Animal Farm, Porton, were used for the majority of the experiments. Albino mice, cross bred rabbits, guinea-pigs, mongrel dogs and bitches, and a few cats were also used.

DNOC.—This was purified by recrystallization from 50% alcohol. It was administered as a 1% solution in weak sodium carbonate solution adjusted to *p*H 7 with hydrochloric acid.

The solution was given in the majority of cases by subcutaneous injection. The drug is very rapidly absorbed and the solutions do not irritate the tissues.

When administered in feeding experiments, measured quantities of a dilute DNOC solution were mixed with weighed quantities of a powdered rat diet to give a known final concentration of DNOC intimately mixed with the food. The daily intake was calculated from the known average intake of food by the rat.

Histology.—Tissues were fixed in formol saline and Helly's solution and prepared in the usual way. Haematoxylin and eosin and certain special stains for glycogen and mitochondria were used.

Results

Lethal Dose and Signs of Acute Poisoning.—The average lethal dose of DNOC administered by subcutaneous injection in a single dose was very much the same for rats, mice, rabbits, guinea-pigs, and dogs. The L.D.50 was calculated for rats and mice and found to be 24·6 (fiducial limits—23·1—26·1) and 24·2 (fiducial limits—21·5—27·3) mg. DNOC per kg. respectively.

After injection of 20 mg. per kg., rats behave normally for 10 to 15 minutes. The rate of respiration then begins to increase rapidly, and within the next 15 minutes the animal is lying prostrate on its belly. It usually lies quite still except for an occasional fine convulsive movement. This condition persists for one to two hours with a gradual recovery. Within four hours the animals are again active, and by 18 hours appear perfectly normal. If food is left in their cage they eat voraciously as soon as they have recovered sufficiently to move about. However, over a 24-hour period their food consumption is not measurably greater than that of normal rats.

Where the dose of DNOC proves fatal, the respiration rate continues to increase after the animal has become prostrate. Death may be preceded by a few convulsive gasps, or it may take place quietly with nothing but a slight outstretching of the limbs to mark it. As a rule muscular rigidity develops just before death, and is complete when the animal dies. This muscular rigidity is a very striking feature and persists for some hours after death. A few observations were made on changes in rectal temperature in poisoned rats. The changes were very irregular, but death can occur in the absence of any hyperpyrexia.

Death usually takes place within two hours of the administration of doses around the L.D.50. Observations on 109 rats that died after a single injection of 20 to 25 mg. DNOC per kg. showed that 76% were dead within two hours, and 91% within five hours. Deaths delayed for 18 hours or more were never observed.

Mice, rabbits, and dogs react in a way very similar to that of the rats except that dogs usually vomit within two hours of receiving a toxic dose. Delayed deaths were not seen in these species.

Effects of Repeated Doses.—The effects of a single dose of DNOC clearly were shortlived, and the animal either died within a few hours or recovered completely. This has an important bearing on the problem of the possible cumulative effects of DNOC. This problem was investigated by giving rats a series of daily doses of 20 mg. DNOC per kg. for periods extending up to six weeks. In the earlier experiments, the injected rats were kept in the warm laboratory. Under these conditions it was found that 5 to 15% died shortly after the injection on any of the first four days, but thereafter only a very occasional acute death was noted even though the injections were continued for three weeks. In later experiments, it was found that significantly fewer rats died if their cages were placed in a cool draughty corridor immediately they had received the DNOC. The figures for these and the earlier experiments (Table 1) show that when the doses are given at successive intervals of 24 hours there is no evidence of cumulative action as judged by the death rate following the injections.

If, however, the interval between consecutive doses is shortened, a cumulative action for DNOC can be demonstrated in both rats and rabbits. A single dose of 5 mg. per kg. of DNOC produces no visible signs of poisoning, but when hourly injections are given characteristic signs of poisoning appear after the fourth or fifth injection. At first, symptoms are shortlived and disappear before the next injection is due. Later they last longer, and the animal dies shortly after an injection. Death takes place in both rats and rabbits after the total dose administered amounts to 25 to 35 mg. per kg. This is the size of a lethal dose when given as a single injection. The similarity of behaviour in this respect in these two species is of interest because, as will be shown later, the rate of disappearance of DNOC from the blood stream is different.

As rats can survive a long series of injections of 20 mg. per kg. of DNOC daily as recorded above and in Table 1, and as almost all the deaths occur

TABLE 1

INCIDENCE OF DEATH AMONG RATS RECEIVING DAILY DOSES OF 20 MG. PER KG. DNOC

Experiment	No. of Injections	No. of Rats	Deaths		Day of Deaths (No. of Animals in Brackets)			
			Total	Per-centage				
1. Rats in warm* laboratory	17	87	27	31	1st (10)	2nd (4)	3rd (11)	4th (2)
2. Rats in cool* corridor *a*..	10	110	4	3·6	2nd (2)	5th (1)	7th (1)	
b..	20	62	4	6·5	4th (3)	5th (1)		
c..	36–45	23	2	8·5	4th (1)	21st (1)		

* Difference between "warm" (1) and "cool" (10 injections) (2a) was highly significant $\chi^2 = 27{\cdot}48$ $P < 0{\cdot}001$
Difference between "warm" (1) and "cool" (20 injections) (2b) was highly significant $\chi^2 = 13{\cdot}23$ $P < 0{\cdot}001$
Difference between "warm" (1) and "cool" (36–45 injections) (2c) was significant $\chi^2 = 4{\cdot}69$ $P = 0{\cdot}03$

after the first few injections, the possibility arises that tolerance to DNOC can be developed. This question was examined by taking the survivors of the series of injections of 20 mg. per kg. and giving them a single dose of 30 mg. per kg. The mortality rate of these animals was found to be lower than that of a control group given the single injection of 30 mg. per kg. This could be taken as evidence of the development of tolerance, but there is the alternative explanation that the previous injections weeded out the susceptible rats and left a selected group of resistant rats. Further, the fact that symptoms of poisoning following the injection of a dose of 20 mg. per kg. DNOC show no appreciable amelioration at the end of a long series of injections points to the absence of any tolerance in animals exposed to repeated doses.

In spite of the severe symptoms of poisoning produced each day by a series of such injections, the rats show no evidence of any serious constitutional disturbance. On an unrestricted diet, rats submitted to such treatment with DNOC do not invariably lose weight, and may have ample amounts of adipose tissue after 45 successive injections of 20 mg. per kg. per day.

Dogs given daily doses of 5 and 10 mg. per kg. for 12 successive days showed no evidence of cumulative poisoning.

When DNOC was administered in the diet of rats, cumulative poisoning was only observed when the calculated daily intake of the drug greatly exceeded the single lethal dose.

At a level of 200 parts per million of DNOC in the diet giving a calculated intake of 15 mg. per kg. per day, rats grew normally over an observed period of 18 weeks. When the calculated dose was 30 mg. per kg. per day no symptoms appeared in rats eating this diet for two and a half weeks, but within four days of doubling the quantity in the food the rats became obviously ill, and four out of 12 rats were dead within 10 days.

Pathological Changes.—Tissues from 78 rats have been examined by both routine and special histological methods. Material was obtained from rats dying after a single large dose, and from animals killed or dying after a series of injections.

Kidney.—The presence of protein in the glomerular filtrate was a constant feature where rats died after a dose of 25 to 30 mg. per kg. Animals killed or dying after smaller doses never showed this protein. The same changes were found in rats dying of overheating and it may therefore be the result of hyperpyrexia.

Liver.—No sign of cellular damage has been found in the livers of rats killed or dying after either single or repeated injections of DNOC. In animals killed up to 48 hours after the last of a series of injections, the lobular pattern of the liver was lost. The parenchymal cells were swollen and packed together. Special staining showed them to be filled with glycogen. When the rat died of acute poisoning, the findings were variable; of 18 livers from such animals, eight had little or no glycogen, while 10 showed increased storage of glycogen. There was no increased storage of glycogen in the tubules of the kidney, in the adipose tissue or in heart muscle. The mitochondria of the liver cells, stained by Altmann's method, were apparently normal, but when the cells were packed with glycogen, the mitochondria were distributed round the periphery and round the nucleus.

Lungs.—When animals died after DNOC or were killed when showing symptoms, there was an intense pulmonary congestion and slight pulmonary oedema.

Adipose Tissue.—In two special experiments the adipose tissue of the testicular omentum and interscapular pad (brown fat) were examined. No histological changes could be detected in the fatty tissue even after a series of 15 daily injections.

The spleen, thymus, thyroid, cardiac and voluntary muscle showed no consistent or unusual variation from the normal.

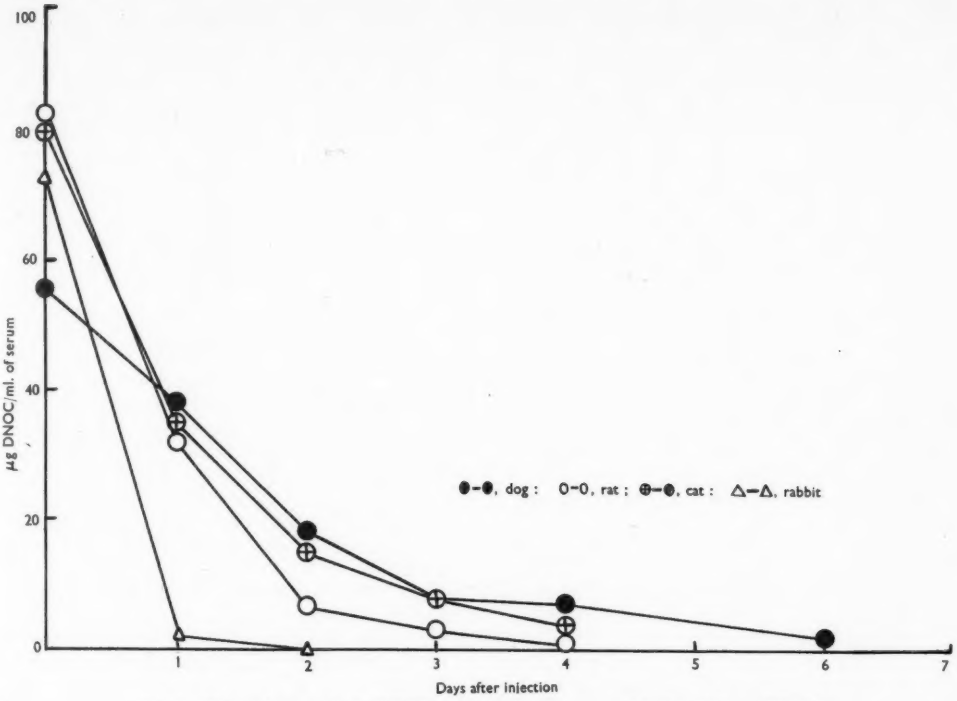

FIG. 1.—Changes in serum level of DNOC after a single subcutaneous injection of 10 mg. DNOC/kg.

Fate of Injected DNOC.—The existence of a simple and accurate method for estimating small quantities of DNOC in the tissues and body fluids enabled the distribution of DNOC after its subcutaneous injection to be studied.

Blood Levels.—The blood level of DNOC was determined in rabbits, rats, cats, and dogs after the subcutaneous injection of DNOC. Over 90% of the DNOC was in the plasma, and only small quantities were found in the red blood cells. It was possible to take serial samples from the larger species, but as a minimum of 2 ml. of blood was required, a rat had to be sacrificed to obtain enough blood for each determination. The figures for blood levels in rats were obtained by taking the mean value for the blood samples from a group of four rats which had been similarly treated, and had been killed at the same time.

Curves showing the changes in blood level after a single injection of DNOC given to rats, rabbits, dog, and cat are given in Fig. 1. The curves are exponential in character. The rate of fall in the blood level of DNOC differs in the various species. The time taken for the DNOC level in the blood to fall to half its initial value after a single injection of 10 mg. DNOC per kg. is in the rabbit about three hours, in the rat 15 hours, in the cat 20 hours, and in the dog 36 hours.

It will be seen in Fig. 1 that after 24 hours the blood level in the rabbit is virtually zero. If the rabbit is given a series of injections on successive days, the rate of fall in the blood level of DNOC remains unchanged on each successive day (Fig. 2). In the rat, the rate of fall after a single injection is slower and as much as 30 μg per ml. of DNOC remains in the blood 24 hours later. Despite this residue in the blood it is not possible to produce a progressive rise in the blood level by giving a series of injections at 24-hour intervals. If the rats are given a second injection 24 hours after the first injection of DNOC, the blood level still falls to the same level 24 hours after the second dose as it did after the first dose. The dog behaves in the same way as the rat, and when given a series of daily injections of 10 mg. per kg. on five successive days, the blood level 24 hours after each injection did not fluctuate significantly.

Furthermore, it was found that after the administration of DNOC had stopped, the rate of disappearance of DNOC from the blood of the dog was exactly the same whether the animal had received one or a number of daily injections beforehand

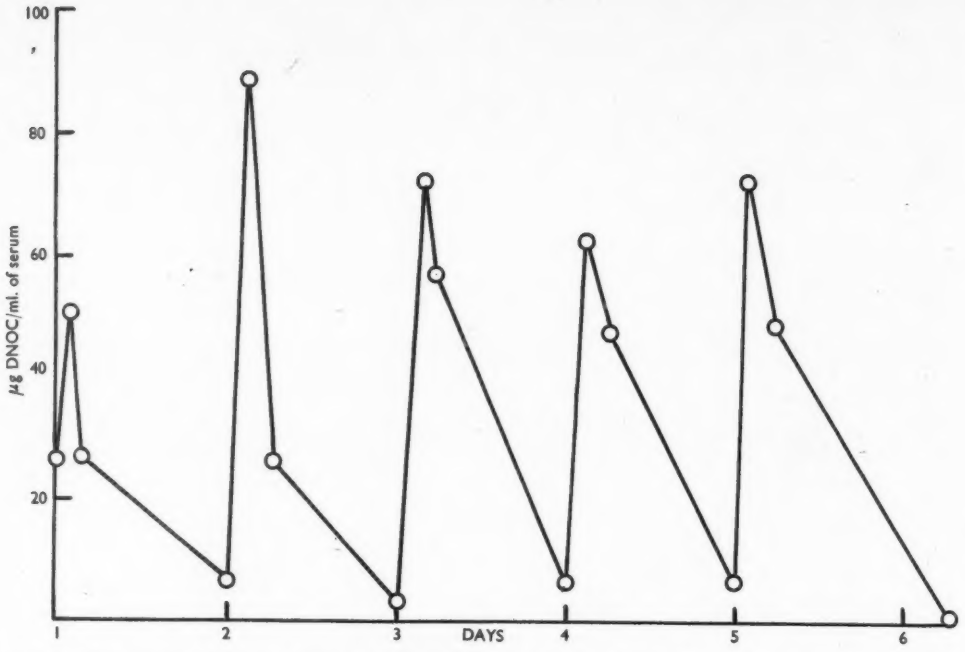

FIG. 2.—Effect of repeated subcutaneous injections (10 mg. DNOC/kg.) on serum level of DNOC in rabbit. Samples of serum analyzed immediately after injection and then at one, three, five, and 24 hours.

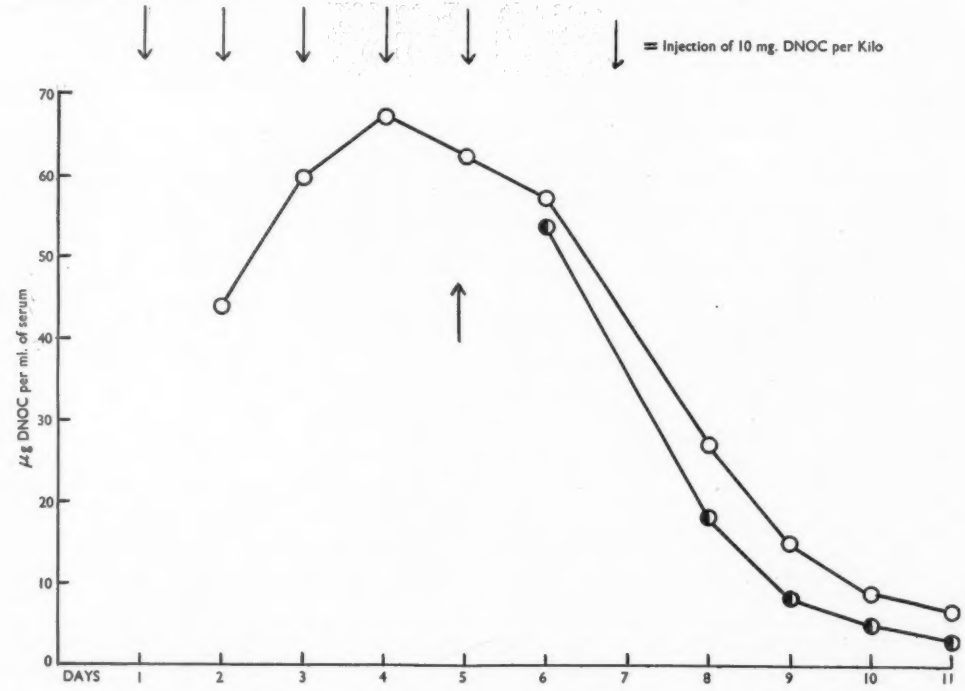

FIG. 3.—The upper curve shows the effect of five daily subcutaneous injections on the DNOC concentration in serum of dog (serum samples taken 24 hours after the previous injection). After the fifth day, no further injections were given.
The lower curve shows the rate of fall of DNOC in serum following a single injection 24 hours before the first sample was taken.

(Fig. 3). The rat behaves in a similar way (see below and Table 3). There is no evidence of an accumulation of DNOC in the blood of dogs, rats and rabbits receiving a series of daily injections of DNOC.

The persistence of a certain amount of DNOC in the circulating blood, 24 hours or more after the last injection of the drug in the dog and the rat, does not reflect any greater susceptibility of these species to further injections. DNOC is cleared much more rapidly from the blood of the rabbit than from the rat. But if rats and rabbits are given hourly injections of DNOC in doses of 5 mg. per kg. they both behave similarly. The same total dose, 25 to 35 mg. per kg., is lethal to each species and they die with blood levels of approximately the same height (125 μg per ml.).

One explanation of the persistence of an appreciable part of the injected DNOC in the blood of the dog and rat for some days, is that this DNOC is fixed to the circulating plasma protein, and that it is only slowly released from this attachment. DNOC will readily attach itself to serum proteins *in vitro*. But there is no evidence from *in vitro* experiments that the plasma protein of the rabbit was less efficient in binding DNOC than the rat. Thus, at a concentration of 100 μg DNOC per ml. in 5 ml., 1 ml. of rabbit serum adsorbed 65% of the DNOC whereas 1 ml. of rat serum only adsorbed 48%. The explanation of the more rapid disappearance of the DNOC from the blood of the rabbit must be independent of the power of the plasma protein to bind DNOC.

Distribution of DNOC in the Tissues.—Rats were given a subcutaneous injection of 10 mg. per kg. and killed by guillotine at intervals afterwards. The amount of DNOC present in the serum and in the brain, spleen, kidney, liver, muscle, heart, and lung was determined. The results are given in Table 2.

It will be seen that the concentration of DNOC in the serum is outstandingly high by comparison with that in other tissues. The high figures for the DNOC content of the lungs and heart may have been due to their relatively high blood content in relation to the weight of the whole organ. The heart was removed *in toto*, and dropped into the tube for homogenization without any preliminary washing to free its cavities from blood. It will be seen that there was no evidence of the accumulation of DNOC in any particular tissue.

From a knowledge of the weights of the different tissues and organs, and assuming the blood to be 6% of the body weight, it was possible to calculate that within 30 minutes of the injection of 1·5 mg. DNOC, 0·725 mg. could be recovered from the animal, and 83% of this was in the blood. After six hours 0·37 mg. could still be accounted for, and at least 72% of this was in the blood. By this time all the acute symptoms of poisoning had disappeared.

The DNOC content of the liver and kidneys of rats was also determined in animals that had received a long series of daily injections of 20 mg. DNOC per kg. The figures are given in Table 3, and show that the concentration of DNOC in the blood, liver and kidneys, 24 hours after the last injection of a dose of 20 mg. per kg. DNOC was the same in animals receiving a single injection as in those that had received 40 successive daily injections.

In other animals the levels in the liver, kidney, and blood were compared 24 and 48 hours after the last injection of DNOC, and again there was no difference in the rates at which the animals could rid their tissues of DNOC whether they had received one or 40 successive injections. There was thus no evidence of accumulation of DNOC in the tissues or, after long exposure to DNOC, of any alteration in the rate at which the animal metabolised DNOC.

Excretion.—The excretion of DNOC in the urine of rabbits and dogs that had received either single or multiple injections of DNOC was studied. The total quantity of DNOC administered ranged from 0·5 to 80 mg. The urine was collected during the days the injections were given, and for the three days succeeding the last injection. Between four and 10% of the total DNOC injected was recovered from the urine as DNOC. There was no significant difference between the amounts recovered from the dogs and from rabbits despite the more rapid fall in the blood level that is observed in the rabbit.

In no case was a positive Derrien test obtained on the urine of either the dog or rabbit. This test is thought to show the excretion of amino-nitrophenol, a conjectural metabolite of DNOC. Tests for glucuronides were negative. The estimations for ethereal sulphates showed there was no significant increase in the amounts excreted by the animals that had been injected with DNOC. These estimations were done to examine the possibility that DNOC or a breakdown product might be excreted in a form combined with glucuronic acid or as an ethereal sulphate. There is no evidence of this.

Factors Affecting the Susceptibility of Rats to DNOC.—Male and female rats whether young or old are equally susceptible to a single toxic dose of DNOC. So also are well-fed rats with continued

TABLE 2

DNOC CONTENT* OF BLOOD AND TISSUES OF RATS KILLED AT INTERVALS AFTER SUBCUTANEOUS INJECTION OF ONE DOSE OF 1·5 MG. DNOC

Time after Injection	Serum	Brain	Spleen	Kidney	Liver	Muscle	Heart	Lung
30 mins.	100	1·5	4·0	7·5	14·0	0·5	8·0	18·0
1 hr.	89	3·5	4·0	7·5	12·0	2·0	13·5	20·0
2 hrs.	97	2·0	4·5	11·0	10·5	0·0	19·0	20·5
3 hrs.	93	4·0	8·0	11·0	11·5	3·5	14·0	15·5
4 hrs.	79	3·5	3·0	4·5	13·5	0·5	13·0	14·0
5 hrs.	76	2·0	4·0	4·5	8·5	2·0	14·0	14·5
6 hrs.	45	3·0	1·5	7·5	8·5	1·5	10·5	30·0

* DNOC content of tissue=μg./1g. wet weight.

TABLE 3

COMPARISON OF DNOC CONCENTRATION IN SERUM, KIDNEY, AND LIVER OF RATS AFTER SINGLE AND 40 SUCCESSIVE DAILY INJECTIONS EACH OF 20 MG. DNOC PER KG.

Treatment	No. of Rats	Concentration of DNOC 24 Hours after Last Injection (μg/g. wet wt.)		
		Liver	Kidney	Serum
a. One injection	19	8 ± 0·7 μg*	7 ± 0·2 μg	45 ± 1·6 μg
b. 40 daily injections	9	7 ± 0·3 μg	7 ± 0·3 μg	38 ± 1·0 μg

* Results expressed as means and standard errors.

access to food, and under-fed rats when the dose of DNOC given was adjusted to their body weight.

Alcohol was given to rats as a 10% solution as their sole source of fluid for three days before and immediately after the injection of 20 mg. per kg. DNOC. The toxic action and rate of recovery from the effects of the DNOC were not affected. Rejsek (1947) has stated that in man, alcohol may cause a recrudescence of the symptoms of poisoning after meta-dinitrobenzene. Although dinitrobenzene does not resemble DNOC in its mode of action, it was thought possible that alcohol may affect adversely poisoning with aromatic nitro-derivatives, in general. An experiment similar to that Rejsek was tried with rats that had received a toxic dose of DNOC. The rats were given 5 ml. of 6% alcohol by stomach tube one, two, and three days after the injection of DNOC. No symptoms other than those attributable to the alcohol were observed.

The effects of heat and cold were also examined. Tainter (1934) claimed that animals kept in the cold were less susceptible to the action of DNP. When the dose of DNOC just borders on the lethal dose this effect of cold is readily observed. As recorded above, it was found that deaths among groups of rats receiving a series of daily injections of 20 mg. per kg. DNOC were reduced from 31% in rats kept in a warm laboratory (Table 1) to between 8·5 and 3·6% when the animals were placed in a cool, draughty corridor.

The effects of greater extremes of heat and cold were also investigated. Rats were injected with various doses of DNOC and then placed in warm or cold rooms for the next four hours. Normal rats kept under the same conditions were not killed. The results are presented in Table 4. The figures show that susceptibility was increased significantly when the animals were kept at 36 to 37°C. A significant degree of protection from the effects of larger doses was produced when the animals were kept at 5 to 10°C.

Discussion

The observations reported in this paper have been made for the most part on animals receiving a lethal or near-lethal dose of DNOC. These doses rapidly produce a severe disturbance of the general metabolism which either proves fatal or else it is completely reversed within a few hours. Such a syndrome of acute poisoning can be produced

TABLE 4

EFFECT OF ENVIRONMENTAL TEMPERATURE ON SENSITIVITY OF RATS TO SINGLE DOSE OF DNOC

Dose of DNOC (mg./kg.)	Environment					
	Cold 5–10°C		Room Temperature 18–20°C		Warm 36–37°C	
	No. of Rats	Mortality (%)	No. of Rats	Mortality (%)	No. of Rats	Mortality (%)
15	—	—	28	0	18	6
20	27	0	88	5	43	60
25	30	23	18	39	—	—
30	18	72	32	97	—	—

Rats were maintained in the hot or cold rooms for four hours after the injection of the DNOC. Deaths all occurred within this four hour period.

Doses corresponding to 50% mortality by converting the mortalities into probits (and using the maximum likelihood solution) are :—

Cold 5–10°C. 27·7 mg./kg. 95% fiducial limits = 26·4—29·7.
18–20°C. 24·8 mg./kg. 95% fiducial limits = 23·7—26·1
36–37°C. 19·2 mg./kg. 95% fiducial limits = 18·0—20·6

day after day for five to six weeks in rats without leading to either cumulative poisoning or the development of any tolerance towards the drug. No histological changes indicative of structural damage to vital organs can be observed. The changes in cardiac and voluntary muscle recently described by Hicks (1950) occur with equal frequency in normal animals.

An increase in the respiratory rate is a constant feature of poisoning by DNOC, and this persists even while the animal is prostrate. Complete prostration was seen constantly in animals injected with a dose of 20 mg. per kg. DNOC, and in these animals only the respiratory muscles and the heart were apparently capable of functioning at the time when poisoning was most severe. Hyperpyrexia is an incidental, but by no means an essential, feature of intoxication by DNOC in rats. Death, when it occurs, appears to result from an acute failure of muscular activity. The animals become prostrate, with rapid, panting respiration. If they are observed carefully it will be found that the skeletal muscles become stiff just before the animal dies. Respiratory and cardiac activity cease simultaneously, and at the moment of death muscular rigidity is complete. An explanation of this sequence of muscular paralysis followed by rigidity can be sought in the recent biochemical studies of the action of DNOC. It has long been recognized that a characteristic action of DNOC on living cells is to increase the intake of oxygen, and this has been found not only in all mammals and birds, but also in preparations as diverse as mitochondria (Loomis and Lipmann, 1948) ; tissue slices (Alwall, 1936) ; sea urchin eggs (Crane and Keltch, 1949) ; and bees (Goble and Patton, 1946). Loomis and Lipmann (1948) threw new light on the problem when they discovered that preparations of kidney mitochondria treated with dinitrophenol (a compound of similar properties to DNOC) took up more oxygen, but failed to combine in the usual way with the phosphate present in the suspending fluid. These observations were extended by Judah and Williams-Ashman (1951), who found that mitochondria poisoned with DNP required increasing amounts of carbohydrate to form organic phosphate esters from inorganic phosphate and that the formation of phosphate esters continuously fell.

A tentative synthesis of these facts can now be made. The oxidation of carbohydrate forms the main source of energy of the body and the energy is tapped off in the form of compounds containing phosphate, e.g. the " high energy phosphate bonds " of adenosine triphosphate (A.T.P.). This compound is then a source of available energy to the body. If DNOC poisoning in the whole animal follows a similar pattern, the formation of adenosine triphosphate would be inhibited. The oxidative processes continue and indeed speed up, but the energy cannot be converted in the body into a useful form, and so it is dissipated as heat. This would account for any rise in body temperature that took place. In the muscle the initial source of energy is believed by many to be the energy-rich phosphate bonds of A.T.P. If the A.T.P. cannot be resynthesised and is progressively broken down to adenylic acid the muscle then goes into rigor. A very similar result was produced first by Lundsgaard (1930) with iodoacetic acid. This compound acts by inhibiting the enzyme triosephosphate dehydrogenase and this also results in the progressive breakdown of A.T.P. and death of the muscle in rigor.

The suggested mode of action of DNOC is consistent with the acute form of poisoning that is observed, but it would form a less satisfactory explanation for any chronic effects on metabolism if these were found. The only evidence of any cumulative effect of DNOC is the slight amount of DNOC that persists for some days in the serum of the rat and the dog. In the dog this may be as high as 60 μg per ml. 24 hours after the injection of 10 mg. DNOC per kg. and its presence does not appear to disturb the dog in any way. It can be calculated that 60 μg. per ml. is three times the concentration that will completely inhibit phosphorylation in mitochondrial preparations but this comparison is a highly artificial and deceptive one.

However, Dr. J. D. Judah (personal communication) has shown that the DNOC in dog serum (at a level of 60 μg per ml.) is still active against mitochondrial preparations, and behaves just as an aqueous solution of DNOC would behave. The naked mitochondria used by biochemists are much more vulnerable than the mitochondria in the cell protected by at least two semipermeable membranes from toxic substances in the blood, and it is probable that considerable extra-cellular concentrations are necessary in order to get any transport of the drug into the cell. The DNOC circulating in the blood of the dog is at least, in part, bound to protein and it is possible that this bound DNOC may not readily pass through all membranes.

The rapid recovery from the effects of DNOC, and the fact that cumulative poisoning does not occur unless the consecutive doses are given within a few hours of each other, suggests that the animal is able to get rid of DNOC rapidly. Only a very small part of the injected DNOC is excreted in the urine, and the conclusion can be drawn that the DNOC must be converted in the body into some inactive material. It is known that the reduction of one of the two nitro groups of DNOC will result in a compound devoid of all the metabolic stimulating properties of DNOC. Homogenized preparations of the liver and kidney will reduce DNOC *in vitro* (Parker, to be published). When an animal has been killed with DNOC, the compound disappears rapidly from the liver after death, but much more slowly from the blood. It is possible that some of the DNOC is reduced in the tissues where it actually exerts its effect upon metabolism, and this is probably the large muscle mass of the body which is so profoundly affected in DNOC poisoning.

Chronic poisoning by DNOC has not been observed in experimental animals, although in the dog, cat, and rat appreciable quantities of DNOC may persist in the blood for several days after a single sublethal dose. These animals do not seem to be any more susceptible to DNOC when the interval between injections is 24 hours. As many as 40 consecutive doses have been administered and under these conditions there is no progressive accumulation of DNOC in the blood. If the doses are spaced closely enough, as with hourly injections, the effects of small doses can be cumulative. The statement that DNOC has no chronic effects is therefore relative, and is used in the usual sense of effects produced days or weeks after the original exposure.

The relevance of these findings to DNOC poisoning in man is difficult to assess. The symptoms of acute poisoning in animals closely resemble those reported in man, and the muscular rigidity that comes on immediately after death in animals has been found in human fatalities (Malter, 1949). The question whether in man the toxic effects of one day's absorption of DNOC can be carried over to the next day cannot be answered by animal experiments, although these suggest that this chronic effect is unlikely. The need for information on the blood level of DNOC in man in the days following the absorption of a non-fatal dose is obvious, but the interpretation of such blood levels may be difficult. Animal experiments have shown that the persistence of DNOC in the blood at levels up to 45 μg per ml. of serum does not appear to increase the susceptibility of the animal to a further sublethal dose. It is apparent that the relation between blood levels of DNOC and symptoms in man may not be simple, and that caution must be observed before any particular blood level is adopted as dangerous or critical.

Summary

The toxic reactions of animals to injections of DNOC are described. A single dose approximating to a lethal dose produces an acute reaction lasting a few hours.

The same dose may be administered at daily intervals for several weeks without producing symptoms or signs of chronic poisoning. Administered at intervals of 24 hours, DNOC shows no cumulative effects nor do rats develop any tolerance towards it.

The blood and tissue levels of DNOC have been examined in rats and the blood levels in rats, rabbits, dogs, and cats after an injection of DNOC.

The effect of alcohol and environmental temperature on the susceptibility of rats have been examined. Small changes of environmental temperature may affect the mortality from a dose of DNOC that is just not lethal at ordinary room temperatures.

The findings are discussed in relation to the behaviour of DNOC in tissues *in vitro*.

We are grateful to Dr. J. O. Irwin of the Statistical Research Unit (M.R.C.) for the figures for the probit analysis given in Table 4.

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VALEUR DE LA TOMOGRAPHIE PULMONAIRE DANS L'EXPERTISE DE LA SILICOSE

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L'application de la tomographie à l'étude de la silicose pulmonaire est relativement récente. Ces dernières années des travaux importants ont, pourtant, paru sur cette question : citons, en particulier, les travaux de Belayew (communication privée) et Zanetti et De Ponti (1949). En France, Leclercq, Balgairies, Bonte, et Declercq (1948) ont précisé les caractères des masses pseudo-tumorales silicotiques (9e Congrès International de Médecine du Travail, Londres 1948). Roche, Naudin, et Tolot, (1949) ont indiqué les résultats de la méthode dans les autres formes radiologiques de cette pneumopathie professionnelle.

La tomographie permet une étude détaillée des organes intra-thoraciques ; il convient de présenter une étude analytique des lésions mises ainsi en évidence.

L'expertise du silicotique se heurte à de nombreuses difficultés pratiques, tant au point de vue diagnostique, qu'en ce qui concerne l'appréciation des troubles fonctionnels ; un exposé synthétique précisera l'intérêt que peut avoir cette technique radiologique pour résoudre les problèmes rencontrés.

Aspects en Évidence par la Tomographie dans la Silicose Pulmonaire

La tomographie permettant une étude plan par plan des organes intra-thoraciques donne de nombreuses précisions sur les altérations produites par la silicose pulmonaire : fibrose du parenchyme et lésions associées (en particulier emphysème, adénopathie trachéo-bronchique).

Cette recherche avait paru utile après constatation de l'aspect parfois différent des lésions anatomiques lors de l'examen macroscopique soigneux de pièces prélevées à l'autopsie, et des images radiographiques.

Atteinte du Parenchyme Pulmonaire.—Les lésions micronodulaires sont, en général, visibles sur les tomographies, dès qu'elles atteignent une certaine intensité ; parfois, même, elles sont plus nettes sur les coupes que sur les films standard.

Dans certains aspects de fibrose paraissant linéaire, sans nodulation nette, la tomographie peut montrer dans les régions sous et rétro-claviculaires, des nodules assez gros, nettement individualisés, localisés dans la partie externe du poumon, ayant l'aspect d'une grappe de raisin vert.

Cet aspect, cette localisation, la bilatéralisation des lésions, paraissent assez caractéristiques de la silicose pulmonaire.

Les macro-nodules sont également très faciles à voir. La tomographie donne des indications sur leur topographie et leur distribution.

Certains ensemencements macronodulaires qui paraissent disposés assez régulièrement sur la radiographie, ont, en fait, une topographie périscissurale. Il convient d'insister sur cette localisation, qui est assez fréquente.

Mais, l' intérêt de cette technique parait primordial au cours des condensations, peu visibles ou invisibles, sur les radiographies.

Dans les aspects appelés nodulaires confluents, images fréquentes dans la silicose, il est difficile, sinon impossible, de préciser l'importance de cette confluence. Pour des images radiologiques analogues la tomographie montre, soit des lésions nodulaires intenses, mais laissant entre elles du parenchyme paraissant sain, soit au contraire, des masses importantes, volumineuses, difficiles à deviner par les techniques habituelles.

Il n'y a pas parallélisme en effet entre l'opacité d'une masse et son épaisseur. Policard (1945) et Martin (1946) ont étudié ces faits, et ont montré que l'opacité radiologique d'une lésion dépend avant tout de l'importance des sels calcaires fixés à ce niveau ; on peut voir une densification progressive d'une image sans modification appréciable de l'aspect et du volume de la lésion.

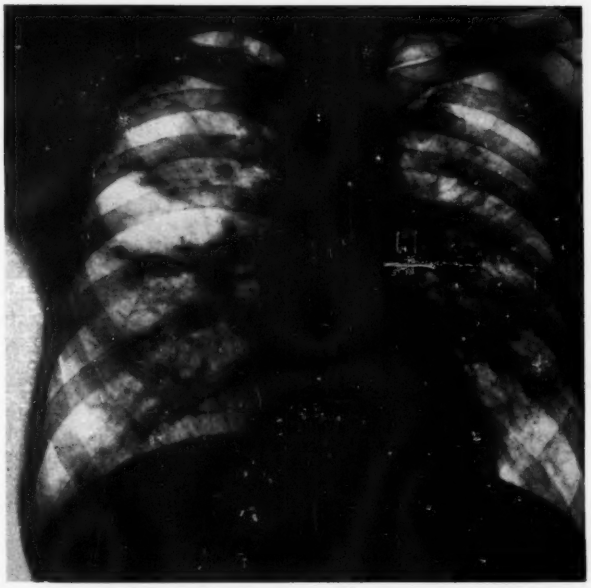

FIG. 1.—C. . . . . ouvrier-céramiste. Radiographie montrant des lésions de fibrose assez atypique ; aspect en voile irrégulier dans la région sous-claviculaire droite.

Le diagnostic de silicose se basait sur les anamnestiques professionnels, l'absence d'évolution radiologique, l'absence de B.K. dans l'expectoration, les signes classiques habituels dans la silicose, en particulier la dyspnée d'effort.

FIG. 2.—C. . . . . Tomographie à 8 cm. du plan dorsal : masses silicotiques bilatérales, et à peu près symétriques. Cet aspect tomographique paraît caractéristique de cette pneumopathie professionnelle.

L'intérêt de la tomographie est d'indiquer en centimètres l'épaisseur d'un bloc silicotique en formation, à un stade où ces lésions donnent une image radiologique très discrète.

Cette méthode permet également de préciser la substratum anatomique d'une image radiologique, non exceptionnelle, appelée " image en voile " ; flou diffus et discret du parenchyme, rencontré dans les régions sous-claviculaires. En particulier, Edme Martin (communication privée) avait depuis longtemps insisté sur cet aspect dans le début de la silicose ; son opacification progressive aboutissait à des images de blocs silicotiques classiques sans qu'existe de lésion nodulaire véritable. Il est à noter que les techniques radiologiques employées à cette époque ne permettaient pas de mettre en évidence les aspects micronodulaires fins, dits " images pinhead ".

Les lésions responsables de cet aspect étaient discutées : scissurite condensation pulmonaire au début.

Dans tous les cas observés, la tomographie a mis en évidence la présence d'opacités parenchymateuses, véritables petits blocs silicotiques, donnant un aspect caractéristique sur les coupes ainsi faites.

Les figures 1 et 2 montrent la radiographie et la tomographie d'un sujet atteint de fibrose pulmonaire, avec aspect en voile assez typique dans la région sous-claviculaire droite ; les coupes montraient un bloc ayant 5 à 6 cm. d'épaisseur (silicose chez un céramiste).

Sur la tomographie, ces blocs silicotiques ont un aspect assez particulier : l'opacité est homogène, ses limites sont nettes, sa topographie particulière, en plein parenchyme, à distance de la paroi thoracique et de la région médiastinale : en effet, on trouve habituellement une zone de parenchyme sain ou emphysémateux séparant la masse du médiastin et du thorax, double couloir clair assez particulier (Fig. 3).

Dans les blocs silicotiques constitués, la valeur de la tomographie est plus restreinte et son intérêt est surtout topographique. Ces blocs sont presque toujours situés de façon assez postérieure et, semble-t-il, au niveau du lobe supérieur. Les tomographies de profil, dont nous avons peu d'expérience, paraissent apporter des renseignements plus utiles.

Il convient, enfin, de signaler que les coupes tomographiques peuvent montrer la présence, à l'intérieur des blocs, de calcifications dont la valeur est discutable : cicatrisation de lésions tuberculeuses anciennes ayant servi de point d'appel à la fibrose pour certains auteurs ; mais il est possible de constater des lésions de ce type bilatérales et symétriques, faisant plutôt penser à des dépôts calcaires secondaires dans des blocs silicotiques.

Lésions Associées.—Sur les coupes tomographiques, il est possible d'observer non seulement l'aspect de la fibrose silicotique, mais également l'état du reste du parenchyme, l'aspect de la trachée et des grosses bronches, des ganglions trachéo-bronchiques.

Les adénopathies trachéo-bronchiques sont souvent augmentées de volume ; il existe parfois une hypertrophie considérable, évoquant une atteinte cancéreuse, type maladie de Hodgkin. Fait important, ces

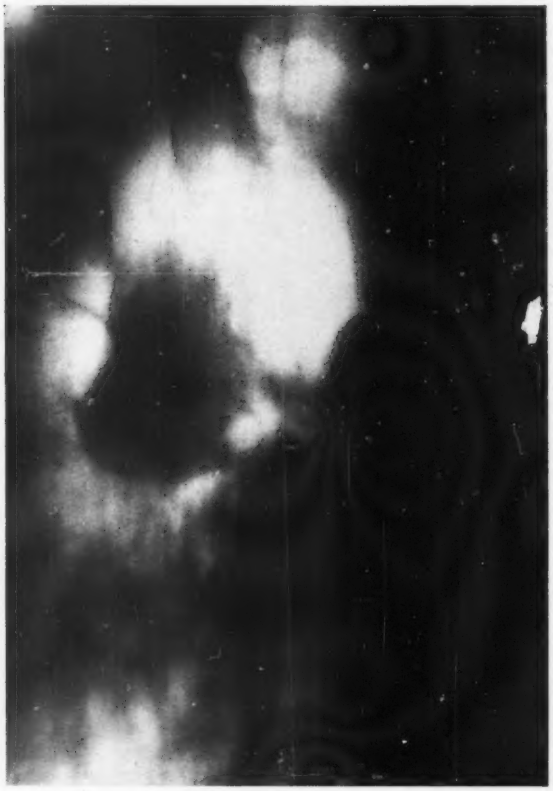

FIG. 3.—G. . . . . silicose chez un mineur au rocher. Tomographie pulmonaire montrant le bloc homogène à limite nette, séparé du médiastin et de la paroi thoracique.

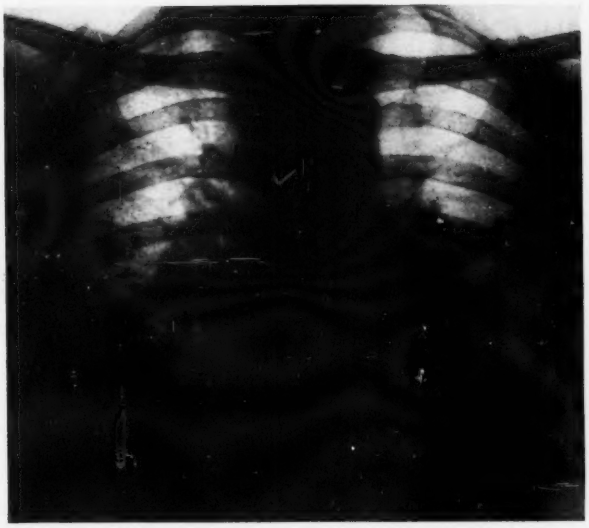

FIG. 4.—L. . . . . décapeur au jet de sable. Radiographie du 11/9/50 : silicose micronodulaire au début : gros hiles.

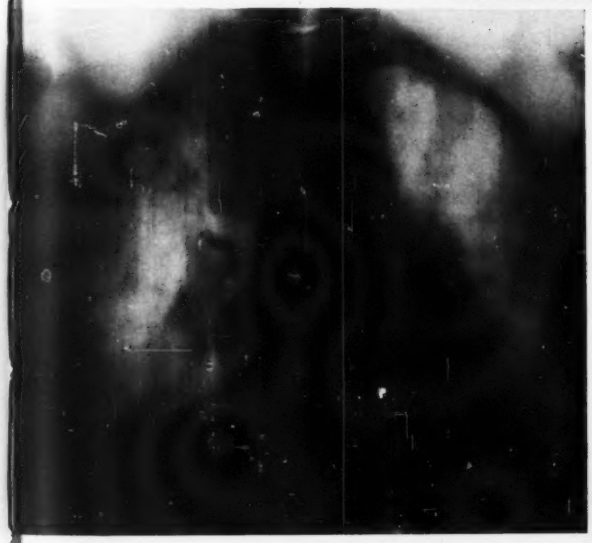

FIG. 5.—L. . . . . Tomographie du 11/9/50 à 9 cm. du plan dorsal : énormes adénopathies trachéo-bronchiques avec petites calcifications anciennes à droite, parenchyme pulmonaire sensiblement normal.

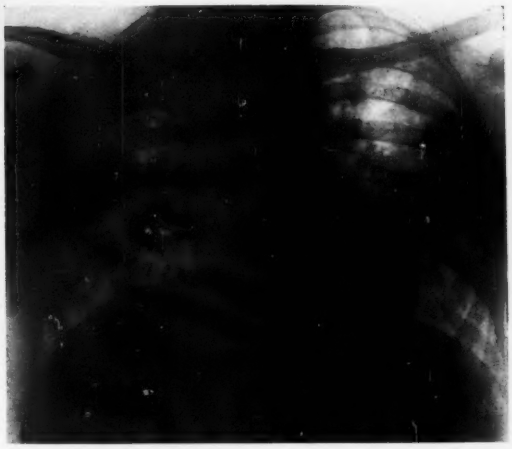

FIG. 6.—L. . . . . Radiographie du 20/4/51 : lésions étendues dans les deux champs pulmonaires. Pas de signes cliniques d'infection, pas de B.K. dans les crachats, dyspnée uniquement à l'effort, état général satisfaisant.

augmentations de volume sont souvent invisibles ou mal visibles sur les radiographies standard. Les figures 4 et 5 montrent la radiographie et la tomographie d'un sujet présentant des signes de silicose au début, avec énormes adénopathies, peu visibles sur le film standard.

A signaler en outre, que les images en coquille d'oeuf, sont souvent plus nettes sur les tomographies que sur les films standard.

L'aspect de la trachée et des grosses bronches doit être étudié avec soin. Habituellement, dans des silicoses avancées, on voit des modifications importantes de l'arbre trachéo-bronchique. La distorsion trachéale, avec attraction le plus souvent droite, est fréquente ; surtout, il existe une ascension très importante de la bifurcation trachéale, appréciée d'aprés la vertèbre dorsale de même niveau ; en outre, les bifurcations des gros troncs bronchiques, dans les hiles, sont attirées vers l'extérieur, et situées non pas le long de la colonne vertébrale, mais à une certaine distance à l'intérieur du parenchyme pulmonaire.

Toutes ces modifications sont une preuve des altérations importantes de l'architecture normale du poumon par la sclérose silicotique ; elles s'observent, ainsi qu'il a été mentionné précédemment, dans les formes avancées de la maladie.

L'emphysème est une lésion précisée par la tomographie.

Il peut être périlésionnel, autour des condensations observées ; il donne parfois des images claires, à bords nets, dont le diagnostic, avec une caverne, est délicat.

Les lésions peuvent être diffuses dans le parenchyme, donnant des irrégularités dans l'opacité du parenchyme, vue sur la coupe tomographique.

Mais surtout, les importants emphysèmes de base, si fréquents dans les silicoses à un stade avancé, sont caractéristiques ; il existe parfois des bulles volumineuses, souvent des irrégularités diaphragmatiques avec bandes ou spicules fibreux, perpendiculaires au plan de ce muscle.

On voit parfois se dessiner un réseau partant des hiles, représentant une opacification des bronches ou des vaisseaux ; cette dernière hypothèse paraît plus séduisante, étant donné que ces réseaux se jettent habituellement dans l'ombre cardiaque ; il n'est pas possible de préciser, actuellement, quelle est la valeur de ce signe indiquant probablement un trouble de la circulation pulmonaire.

La tuberculose compliquant une silicose, signée par une expectoration bacillifère, s'accompagne habituellement de lésions cavitaires ; elles sont souvent invisibles sur le film standard, mais facilement trouvées sur les coupes tomographiques ; la caverne paraît en effet exister dans presque tous les cas de silico tuberculose, telle qu'elle vient d'être définie.

FIG. 7.—N. . . . . céramiste. Tomographie de la partie postérieure du hile droit (6 cm du plan dorsal) montrant une caverne, invisible sur la radiographie standard.

La cavité peut être isolée en plein paranchyme apparemment sain (Fig. 7) ou être creusée à l'intérieur d'un bloc silicotique (Fig. 9).

Valeur de la Tomographie dans l'Expertise du Silicotique

Les difficultés rencontrées dans l'expertise du silicotique sont essentiellement de deux types : diagnostic, appréciation de l'incapacité permanente.

Le Diagnostic.—Le diagnostic de la silicose est habituellement aisé ; mais il convient de la différencier de certaines affections pulmonaires qui peuvent s'observer chez des sujets soumis à l'inhalation de poussières, et en particulier la tuberculose fibreuse banale, avec absence du bacille de Koch dans l'expectoration.

FIG. 8.—F. . . . . mineur d'une mine de pyrite. Radiographie standard.

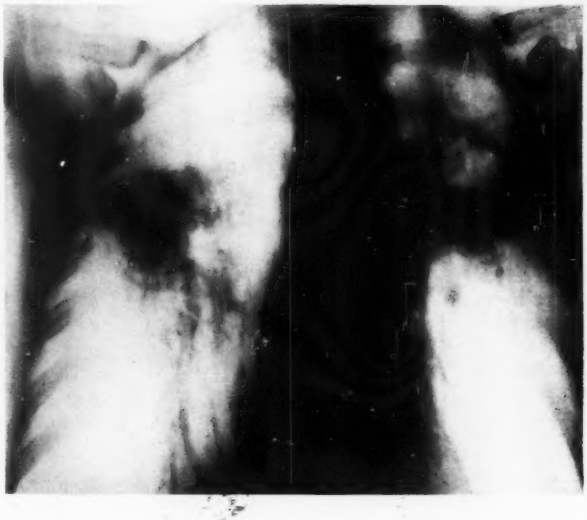

FIG. 9.—F. . . . . Tomographie pulmonaire : blocs silicotiques bilatéraux, avec creusement du bloc gauche par une vaste caverne. L'aspect de cette tomographie paraît typique de la silico-tuberculose, alors que la radiographie était moins caractéristique.

Les masses silicotiques précédemment décrites, visibles seulement, ou surtout, à la tomographie, et donnant radiologiquement soit des images nodulaires confluentes, soit des aspects en voile assez peu caractéristiques, ont une importante valeur diagnostique.

La tuberculose fibreuse paraît donner en effet, à la tomographie, un aspect très différent : les opacités, lorsqu'elles existent, sont peu homogènes, irrégulières, à limites imprécises ; en outre, les lésions sont plus étendues et atteignent habituellement la paroi thoracique ; elles siègent souvent à l'extrême sommet du poumon et sont plus rarement rétro ou sous-claviculaires ; enfin, la bilatéralité et surtout la symétrie, sont rares.

Il est bien évident qu'il n'existe pas d'image véritablement spécifique de la silicose ; une image analogue à celle rapportée par la figure 3 peut se voir au cours d'une tuberculose banale : c'est l'aspect d'un tuberculome ; mais, une telle lésion, exceptionnelle au cours de la tuberculose, est habituelle dans la silicose ; sa valeur diagnostique, quoique relative, est grande.

La valeur diagnostique de ces lésions bilatérales et symétriques parait très importante en cas de topographie anormale ; il a été possible d'observer un ouvrier, carrier, qui présentait une opacité assez irrégulière et étendue au niveau de la base droite, sans lésion précise du côté gauche, évoquant le cancer pulmonaire. Les tomographies montraient à droite un gros bloc ayant les caractères du bloc silicotique et à gauche, masqué en partie par l'ombre cardiaque sur la radiographie, un petit bloc du même type : un tel aspect permettait d'affirmer l'existence d'une silicose, diagnostic confirmé ultérieurement par la vérification anatomique.

A noter la valeur de lésions nodulaires nettes, à topographie assez régulière, montrées par les coupes dans certaines formes de fibrose typique.

Le diagnostic de la silico tuberculose pose également des problèmes difficiles : sont considérées comme telles, dans la législation française, les complications tuberculeuses d'une silicose préexistante avec présence du bacille de Koch dans les crachats.

Il faut donc distinguer cette forme de la tuberculose banale de l'ouvrier exposé aux poussières : la présence, à la tomographie, de blocs, souvent creusés, (Fig. 9), est un argument d'importance en faveur de ce diagnostic.

Enfin, actuellement, certaines silico-tuberculoses sont traitées par la streptomycine, bien que l'indication de l'antibiotique soit parfois critiquable ; cette thérapeutique, négative souvent la bacilloscopie ; dans ces conditions la constatation d'une caverne permet de porter le diagnostic ; il en était ainsi dans le cas de N. (Fig. 7).

Valeur de la Tomographie.—Dans l'appréciation des troubles fonctionnels la valeur de la tomographie est encore plus importante.

La dyspnée dépend, en effet, de nombreux facteurs : la destruction du poumon par la fibrose et l'emphysème associé paraît avoir, pourtant, un rôle capital ; sans vouloir la négliger, l'influence des autres facteurs (atteinte bronchique, spasme, lésions vasculaires), paraît plus accessoire.

Il est classique d'admettre qu'il n'y a pas de parallélisme entre lésions radiologiques et troubles fonctionnels. Ceci est exact si on entend par lésions radiologiques uniquement des opacités parenchymateuses dûes à la silicose. Mais, lorsqu'on tient compte des lésions associées et surtout de l'emphysème, et qu'on apprécie la destruction du parenchyme pulmonaire, il existe, habituellement, un parallélisme étroit entre manifestations fonctionnelles et atteinte radiologique.

La tomographie permet d'apprécier de façon précise ces deux éléments : l'intensité de la fibrose pulmonaire et en particulier, l'étendue des masses peu visibles sur la graphie ; on peut préciser l'épaisseur de ces masses : certaines pseudo-tumeurs denses, représentent parfois la destruction d'une partie relativement minime du poumon, et ont un volume bien moindre que celui de certaines nodulaires confluentes : il n'est pas étonnant que dans ce dernier cas la dyspnée soit plus grave que dans le premier. Le second élément que la tomographie permet d'apprécier est l'importance de l'emphysème

FIG. 10.—M. . . . . (mineur au rocher.) Tomographie à 10 cm. du plan dorsal : blocs silicotiques importants, lésions d'emphysème associé intenses, ces dernières donnent une hyperclarté de la coupe tomographique, caractéristique sur le film, mais la reproduction sur papier n'est pas satisfaisante.

associé également capital. On se rend compte, par la tomographie, de l'intensité et de l'étendue de ces lésions destructrices.

Certains sujets ne présentent, pratiquement, plus de parenchyme sain ; on peut se demander comment ils peuvent garder une hématose compatible avec la vie : la figure 10 est une preuve de ces destructions presque complètes des poumons.

Dans le taux d'incapacité, le facteur pronostic joue un certain rôle : il nous semble que l'hypertrophie importante des adénopathies trachéobronchiques s'observe dans certaines silicoses évolutives ; l'observation de L. en est un bel exemple : il suffit de comparer les deux radiographies faites à six mois d'intervalle. (Il est à noter qu'un traitement à la streptomycine avait été prescrit chez ce sujet, malgré l'absence de signe clinique de tuberculose, sans résultat.) Cette constatation qui paraît d'une certaine gravité à donc des conséquences pratiques.

Le diagnostic de silicose entraine de telles conséquences dans la vie professionnelle d'un ouvrier, l'appréciation exacte des troubles fonctionnels a une telle importance, non seulement pour la réparation de la maladie, mais pour le reclassement du sujet, que l'expertise du silicotique doit s'entourer de toutes les garanties possibles : or, les difficultés sont nombreuses, en particulier quant à l'estimation de l'incapacité ; les épreuves fonctionnelles pulmonaires, qui rendent de grands services, ne sont pas pleinement satisfaisantes ; aussi, parait-il utile de faire, toutes les fois que c'est nécessaire, des tomographies pulmonaires.

Cette technique est demandée après avoir vu la radiographie et surtout fait une radioscopie : ces deux techniques permettent de préciser dans quels cas la tomographie est intéressante, le nombre et la profondeur des coupes demandées. L'association de ces trois méthodes radiologiques est précieuse et permet souvent, associée seulement à un examen clinique soigneux, d'apprécier de façon pleinement satisfaisante l'importance de l'invalidité secondaire à la pneumopathie professionnelle.

L'experience d'une centaine d'expertises m'a convaincu de la valeur pratique de cette méthode lorsqu'elle est employée à bon escient.

English Summary

The importance of tomographic studies in silicosis is described and illustrated by allusion to representative cases.

It is stressed that an exact evaluation of the extent of the disease can only be made by using the three radiological aids : radiography, fluoroscopy, and tomography.

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"ENTENTE RADIOLOGIQUE"

A STEP TOWARDS INTERNATIONAL AGREEMENT ON THE CLASSIFICATION OF RADIOGRAPHS IN PNEUMOCONIOSIS

BY

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Advance in our present understanding of the natural history of pneumoconiosis and of our knowledge of its prevalence in various dusty occupations can only be achieved if workers in different countries and within each country can reach some agreement on radiological diagnosis and classification.

For this purpose the following requirements must be met.

There must be an agreed system of description and classification of the radiological appearances.

Different observers must be able to apply the system of classification thus agreed in such a way that they will classify a given series of radiographs into the same categories. Fletcher and Oldham (1949 and 1951) have shown that agreement in the use of a radiological classification of pneumoconiosis cannot be achieved without taking special measures. To reduce inter-observer error they suggested both the use of standard films and also a system of duplicate consultative readings.

The radiographs used by different observers must be of a uniform and high technical standard. Results obtained by the use of miniature radiographs cannot be compared with the results obtained by full size films (Schepers, 1950 ; Fletcher, 1951). Even with full-size films, technical differences will result in considerable differences in classification (Fletcher and Oldham, 1949). It is essential that where comparisons are to be made between the prevalence of disease in two different populations, the radiological technique used should be the same throughout both populations.

In this paper we shall describe recent attempts we have made to achieve some degree of international agreement on a system of radiological classification for the pneumoconioses. The work is still in progress, and this is in the nature of an interim report which may encourage observers other than those already concerned to join in the field of agreement.

In 1949, there was serious divergence among the methods adopted by different workers in Europe for the radiological classification of pneumoconiosis. In Great Britain, the classification proposed by Davies and Mann (1949), and by Fletcher, Mann, Davies, Cochrane, Gilson and Hugh-Jones (1949) was superseding that proposed by Hart and Aslett (1942), and was becoming generally accepted. This classification distinguished "simple" and "complicated" pneumoconiosis, and the sub-divisions of the former were based predominantly on the profusion and diffusion rather than on the size or type of opacity in radiographs. In France and Belgium (van Mechelen, 1950) on the other hand, classifications similar to that proposed by Eck and Hanaut (1944) were generally used. These classifications were based chiefly on the character of the abnormal opacities. Linear, micronodular, and nodular types were separated without regard for the number or profusion of the opacities. The word "reticulation" was used in many countries to imply anything from the earliest to the most advanced abnormality found in pneumoconiosis, in the absence of coalescent shadows.

In Germany (Böhme, 1934 ; Jötten and Gärtner, 1947) ; Switzerland (Schinz and Eggenschwyler, 1947 ; Lang, 1948) ; Holland (Mey, 1947) ; and the U.S.S.R. (Genkin and Molokanov, 1950) classifications based on that recommended by the 1930 international conference on silicosis were used, the disease being divided into three stages, which were separated partly on radiological, and partly on clinical grounds. In Italy (Vigliani, Parmeggiani, and Zanetti, 1948 ; Vigliani, 1950) reticular, early and late nodular, and massive stages were described.

The three-stage classification was also commonly

used in the United States of America (Jones, 1942), but the Public Health Service (Dreesen, Page, Hough, Trasko, Jones, and Franks, 1942) employed a more elaborate system based on the report of the Pancoast Committee (U.S. Public Health Service, 1935). Compromise classifications were also suggested (Garland, 1936). The Japanese (Yamamoto, 1951) also used three stages. In Australia (Outhred, 1949 ; George and Wallman, 1949) increased linear markings or reticulation, early or nodular pneumoconiosis, and well developed pneumoconiosis were described.

South African workers continued to use the system published by the Miners' Phthisis Medical Bureau in 1936. This separated " simple " and " infective " silicosis, and recognized eight different stages of the simple disease, ranging from increased linear markings to large mottling.

This account of existing forms of radiological classification is far from comprehensive, but it gives some idea of the extent of international confusion which existed when, in February, 1950, the International Labour Office held a conference of experts on pneumoconiosis in Sydney. This conference had the question of radiological classification of pneumoconiosis on its agenda. It finally accepted by a majority vote a scheme of classification, given in full in Appendix 2. It will be seen that it is similar to that proposed by the Pneumoconiosis Research Unit of the Medical Research Council (Fletcher and others, 1949), in that it recognizes a broad distinction between films with only disseminated, more or less circular opacities, and those with coalescent or massive shadows, and it bases the sub-division of the simple or nodular forms of pneumoconiosis on the profusion and diffusion of the opacities rather than on their size, while leaving room for sub-divisions according to their size or other characteristics.

In the summer of 1950 we wished to compare the prevalence of pneumoconiosis in certain British coal mines at which we had carried out surveys, with the reported prevalence at coal mines in the North of France (Declercq, Balgaires, Flouquet, and Morel, 1949). We therefore suggested a joint study of the classification of radiographs between workers in South Wales and in the North of France. In August, 1950, two of us (A.L.C. and I.D.) visited Douai taking 200 films of South Wales coal miners which had already been classified according to the P.R.U. scheme. These films were then classified by Drs. Balgaires, Aupetit, Declercq, Foubert, Jarry, and Nadiras in Douai according to their system of classification, while a group of films which they had already classified by their method was read by Drs. Cochrane and Davies. The two classifications applied to these groups of films were then compared, and it became clear that they were similar in important respects. There was, for example, almost complete correspondence between the British and international categories B, C, and D of massive fibrosis and the French "pseudo-tumorales", and also between the category A of early massive fibrosis and the French category of " confluence ".

On the other hand, the classification of the films which the British called " simple pneumoconiosis " was quite different. The French classified these films, according to the dominant morphological type and size of the opacities, as " pinhead ", micronodular, and nodular ; the British paid attention chiefly to their profusion and recognized lesser degrees of abnormality than the French, who read the British category 1 films as normal, *reticulation* or *fibrotique*. The approximate equivalents of the two classifications are given in the extreme left hand and right hand columns of Table 1. After some discussion, it was agreed that for a trial period, the

TABLE 1

APPROXIMATE EQUIVALENT OF BRITISH, INTERNATIONAL, ANGLO-FRENCH, AND FRENCH RADIOLOGICAL CLASSIFICATION OF PNEUMOCONIOSIS

British (P.R.U.)	International (I.L.O.)	Anglo-French	French
0	0	0	N*
1	1	1	R or F
2	2	P 2 M N	Pinhead Micronodulaire Nodulaire
3 4	3	P 3 M N	
	X	X	
A	A	p A m n	C
B C	B C	B C	T
D	D	D	

*N = normale
R = reticulation
F = fibrotique
C = coalescence
T = tumorale

French workers would try to use the British numerical classification as well as their own, and that the British would in turn sub-divide their categories 2 and 3 according to the morphological type of

opacity, category 1 presenting too little abnormality for this sub-division.

During the autumn of 1950, both sets of workers adopted this joint method. In December, 1950, a group of films which had been thus classified by Dr. Cochrane and Dr. Davies was selected with the following approximate distribution of categories according to the British numerical classification :

Category 0	.. ..	25 films
Category 1	.. ..	25 films
Category 2	.. ..	60 films
Category 3	.. ..	60 films
Category A	.. ..	30 films

These films were sent to Douai and were read by Dr. Balgaires and his colleagues according to the joint classification. Both groups of workers read the films on two separate occasions, so that some measure of the consistency of reading could be obtained. In Fig. 1 a comparison is given between the first British and the first French reading on this set of films according to the British numerical classification and according to the French morphological classification. It will be seen that there was agreement on approximately 60% of the films. On the whole, the French tended to allot lower category numbers to the films (i.e. to read less abnormality) than the British. For example, 58 films were called category 2 by the British ; 25 of these were given a lower category by the French and only eight were given a higher category. They tended to read the nodular types with much greater frequency than the British, reading pinhead less often. The extreme divergences shown in Fig. 1a were chiefly due to films read by the British as category A, being considered by the French to show tuberculosis without clear evidence of underlying pneumoconiosis (five cases) or with only very slight changes.

The British read the films according to the numerical category on two occasions with 80% consistency, while the French, with less experience of this method, achieved 70% consistency. In the morphological classification of films with category 2 or more abnormality, the French were 82% consistent, while the British, who placed 77% of the films into the micronodular group, were thus able to achieve 87% consistency.

It was clear that while both groups of readers were using the classification consistently, there were still considerable differences in the readings of the two groups.

In January, 1951, two of us (A.L.C. and C.M.F.) again went to Douai and read the set of films in consultation with Dr. Balgaires and his colleagues. Dr. A. Hanaut, chief medical officer to the *Charbonnages de France*, also took part in this consultative reading. As a result, a final system of classification incorporating the essential features of both British and French systems was agreed. This is given in summary in Table 1 showing the equivalent classification of categories according to the

Fig. 1.

COMPARISON OF FRENCH AND BRITISH INDEPENDENT READINGS

(*a*) NUMERICAL CLASSIFICATION

British Reading \ French Reading	0	1	2	3	A	Total
0	20	2				22
1	18	9				27
2	9	16	25	8		58
3			17	45	1	63
A	5	2	1	3	19	30
Total	52	29	43	56	20	200

(*b*) MORPHOLOGICAL CLASSIFICATION

British Reading \ French Reading	0 or 1	P	M	N	Total
0 or 1	49				49
P	9	10	10	3	32
M	23	4	58	31	116
N				3	3
Total	81	14	68	37	200

In this figure and in Figs. 2 and 3 the numbers are the numbers of films given the classification in the corresponding row and column headings. Thus the diagonal squares show the number of films upon which the readings were in agreement.

original British, French, and the international classification. The full details of the Anglo-French system of classification is given in Appendix 1.

It will be seen that this Anglo-French classification is very similar to the international classification suggested by the conference of the International Labour Organisation at Sydney in 1950 (Appendix 2).

The final Anglo-French classification differed from the earlier joint classification in adding a category X for abnormal films in which the diagnosis of pneumoconiosis was doubtful, and also in allowing for doubt (expressed by " ? ") in classifying the underlying morphological type of pneumoconiosis in cases with extensive confluence.

The Anglo-French differs from the international classification chiefly in that it makes formal provision for classifying the morphological type of appearance into three particular types. The use of category X is also slightly different. Other minor differences lie in the definitions of category 1 and of categories A–D, but these are differences of phrase rather than of essence. It was agreed that the classification could only be fully appreciated by studying illustrative films, rather than by the use of verbal descriptions in isolation.

In Fig. 2, a comparison is given between the French independent reading of the group of films and the final consultative reading, and in Fig. 3 between the British independent reading and the consultative reading. A full comparison is given in section *a* of each figure ; and sections *b* and *c* give an analysis according to the classification on the numerical basis and on the morphological basis. It will be seen that relative to the consultative reading, the French, working by themselves, still tended to give a rather lower numerical classification to the films than the British, and tended to read the nodular type more frequently. The British numerical classification was fairly close to the final agreed classification with a tendency to allot slightly higher category numbers and with a tendency to read pinhead rather more frequently and nodular much less frequently.

It has been noted (Fig. 1a) that there were five films considered by the British to show category A, but which the French had diagnosed as O. This was because they considered these films to show tuberculous shadows rather than confluence. Of these films, four were finally agreed to show simple pneumoconiosis with tuberculous scars, and one was put into category X indicating that the appearances might not have been due to pneumoconiosis at all. The other films placed in category X were four which had been read as category 2 by the British and one read as category 1. These were films showing a dense reticular pattern without any clear-cut opacities characteristic of pneumoconiosis. Category X was found to be very useful for these relatively infrequent films whose interpretation is difficult, but it was agreed that this category should only be used sparingly. It was also interesting that the films placed in category X were all of elderly ex-miners.

It should also be noted in the agreed reading that of the 135 films allocated a category number of 2, 3 or A and thus receiving a morphological reading, 108, or 80%, were read as micronodular (Fig. 2c and 3c). Pinhead films formed only 12% of the total, and nodular only 8%. It thus appears that, at any rate in films of South Wales coal miners, the morphological classification is not very discriminating.

In our discussion concerning the relative importance of the numerical classification according to the profusion of the opacities and the classification according to the type and size of the opacities, the French experts pointed out that in progression of simple pneumoconiosis, there is both an increase in size and number of opacities, as had indeed been found by Davies, Fletcher, Mann, and Stewart (1949), and that confluence leading to massive fibrosis is more likely to occur in films of the nodular type so that the morphological classification

TABLE 2

PERCENTAGE FREQUENCY OF DIFFERENT MORPHOLOGICAL TYPES OF FILMS ACCORDING TO CATEGORY NUMBER

FRENCH READING

Category	Morphological Type			Total
	P	M	N	
2	9 (4)*	63 (27)	28 (12)	100 (43)
3	16 (9)	63 (35)	21 (12)	100 (56)
A	5 (1)	30 (6)	65 (13)	100 (20)

AGREED READING

Category	Morphological Type				Total
	P	M	N	?	
2	16 (9)	80 (43)	4 (2)	—	100 (54)
3	8 (5)	82 (48)	10 (6)	—	100 (59)
A	7 (2)	61 (17)	11 (3)	21 (6)	100 (28)

* Actual number in brackets.

corresponds to the progression of the disease and gives an indication of prognosis.

In Table 2, the morphological classification of all the films placed in categories 2, 3, and A according to the independent French reading and according to the agreed reading is given. It will be seen that in the agreed reading there is no significant difference in the distribution of the three types of opacity in the different numerical categories, although in the French reading the nodular type was read more frequently in category A films. This difference is partly due to the fact that in six of the films of category A which the French readers described as nodular, it was ultimately agreed that the nodular appearance was part of the confluent shadow and that the underlying morphological type was not classifiable. They were therefore described as A? (Fig. 2). It is known (Gough, 1947) that, pathologically, massive fibrosis begins by the formation of collagenous nodules larger than those found in simple pneumoconiosis. These nodules coalesce to form areas of massive fibrosis. This preliminary nodular stage of massive fibrosis may, in radiographs, be mistaken for the nodular type of simple pneumoconiosis. This mistake would naturally lead to the conclusion that there was a special tendency for the nodular type of film to go on to confluence. This confusion may be avoided by recognizing that localized nodular shadows, especially in the upper zones, are usually a sign of early massive fibrosis and that only generalized nodular appearances should be classified as simple pneumoconiosis of the nodular type.

Further studies are required to show whether the classification into pinhead, micronodular, and nodular types has important prognostic or diagnostic significance. It is probable, for instance, that workers exposed to dust with a high silica content are more likely to develop the nodular type of picture.

On the other hand, there is good evidence that the numerical classification is well related to the natural progression of the disease and is of some prognostic importance.

Progression studies carried out by the Pneumoconiosis Research Unit have shown that as the disease progresses, the classification tends to rise from 1 to 2 to 3 although the type of films, i.e. pinhead, micronodular, or nodular, nearly always remains the same. Moreover, in surveys carried out at various mines we have found that as the prevalence of pneumoconiosis increases, so does the frequency of the higher category numbers.

Massive fibrosis has not yet been seen developing in cases of category 1, and it usually appears on a background of the upper limit of category 2 or category 3 (Davies and others, 1949; Cochrane, Fletcher, Gilson, and Hugh-Jones, 1951). Thus the category number has prognostic value.

Against the numerical classification it may be objected that the division of the lung fields into vertical thirds is arbitrary and is unrelated to any anatomical conception. Further, it is known from pathological studies that simple pneumoconiosis is generalized throughout both lung fields from the outset and does not start near the hilum and extend outwards in the course of time.

However, in radiographs the opacities are nearly always first seen in the centre of the lung fields and only appear *in profusion* more peripherally as the disease develops. This is probably due simply to the fact that at the periphery of the lung fields, as they appear in a radiograph film, the rays have had a smaller thickness of lung to traverse before reaching the film. Generalized radio-opaque foci must therefore appear less profuse in the peripheral part of the lung fields.

Thus, the definition of the categories according to the profusion at the periphery has some anatomical basis, but it is important to stress that the fundamental distinction between categories 1, 2, and 3 is based on the *general profusion* of opacities and not only on their diffusion to the periphery. This is one reason why standard films as well as verbal descriptions are essential to enable different observers to agree on the numerical classification of films (see below).

It must be remembered that the classification is based chiefly on experience with radiographs of coal miners who seldom develop unmodified silicosis. The opacities in classical silicosis commonly first appear and may remain confined to the upper zones. In such cases, the provision made in the international classification should be applied, i.e. " in cases where there is an uneven distribution of the opacities in different parts of the lung fields, the category is determined by the most advanced abnormality that is present over at least half of the lung field ".

A meeting was held at Douai in June, 1951, at which this joint Anglo-French classification was presented to doctors concerned with coal-worker's pneumoconiosis from other coalfields in France, from Belgium and from Holland, and at which it was agreed to give the joint classification a trial over a much wider area (Aupetit, Balgaires, Declercq, Foubert, and Nadiras, 1951).

It is important to stress that the existence of an agreed classification does not ensure that the classification will be used in exactly the same way by different observers, as is seen by the disparity which existed between the British and French readings

Fig. 2.

COMPARISON BETWEEN INDEPENDENT (FRENCH) READING AND AGREED CONSULTATIVE READING

(*a*) FULL COMPARISON

Agreed Reading

French Reading	O	I	2 P	2 M	2 N	3 P	3 M	3 N	A p	A m	A n	A ?	X	Total
O	29	9	2	5					1	2			4	52
I	3	12	3	9									2	29
2 P			2	1			1							4
2 M				16			9			2				27
2 N				5	2		2	2		1				12
3 P			1			5	2		1					9
3 M			1	6			27			1				35
3 N				1			7	4						12
A P										1				1
A M										6				6
A N										4	3	6		13
Total	32	21	9	43	2	5	48	6	2	17	3	6	6	200

(*b*) COMPARISON OF NUMERICAL CLASSIFICATION

Agreed Reading

French Reading	0	1	2	3	A	X	Total
0	29	9	7		3	4	52
1	3	12	12			2	29
2			26	14	3		43
3			9	45	2		56
A					20		20
Total	32	21	54	59	28	6	200

(*c*) COMPARISON OF MORPHOLOGICAL CLASSIFICATION

Agreed Reading

French Reading	0+1	P	M	N	?+X	Total
0+1	53	6	16		6	81
P		9	5			14
M		1	67			68
N			20	11	6	37
Total	53	16	108	11	12	200

Fig. 3.

COMPARISON BETWEEN INDEPENDENT (BRITISH) READING AND AGREED CONSULTATIVE READING

(*a*) FULL COMPARISON

Agreed Reading

British Reading	O	I	2 P	2 M	2 N	3 P	3 M	3 N	A p	A m	A n	A ?	X	Total
O	21	1												22
I	11	14		1									1	27
2 P			7	4			1							12
2 M		5		30	1		3	1		2			4	46
2 N														
3 P			2	1		5	6							14
3 M				5	1		37	2		1				46
3 N								3						3
A P		1							1	3		1		6
A M				2			1		1	11	3	5	1	24
A N														
Total	32	21	9	43	2	5	48	6	2	17	3	6	6	200

(*b*) COMPARISON OF NUMERICAL CLASSIFICATION

Agreed Reading

British Reading	0	1	2	3	A	X	Total
0	21	1					22
1	11	14	1			1	27
2		5	42	5	2	4	58
3			9	53	1		63
A		1	2	1	25	1	30
Total	32	21	54	59	28	6	200

(*c*) COMPARISON OF MORPHOLOGICAL CLASSIFICATION

Agreed Reading

British Reading	0+1	P	M	N	?+X	Total
0+1	47		1		1	49
P	1	15	15		1	32
M	5	1	92	8	10	116
N				3		3
Total	53	16	108	11	12	200

before the joint meeting. It is suggested that, in order to ensure that a classification of this kind is used in the same sense by different observers, it will be necessary to have a set of films, such as the 200 used in our consultative reading at Douai, with an agreed classification. This could be sent to different workers who could classify the films according to their own interpretation of the classification, and then compare their results with the agreed opinion. In this way they will be able to ensure that they are using the classification appropriately. The International Labour Office would be a suitable body to collect and hold such a set of films. Joint consultative readings between workers from different centres would do much to facilitate general agreement.

Fletcher and Oldham (1951) have shown that the use of standard films may enable observers who are inexperienced in a particular classification to give the same readings as those given by more experienced observers. A set of standard films appropriate to the joint classification has been collected at Cardiff and Douai. A limited number of sets of films as agreed by the Pneumoconiosis Research Unit are available on application to the Director of the Pneumoconiosis Research Unit, Llandough Hospital, near Cardiff. Both British and French standard films may be consulted on application to Cardiff or to Dr. Balgaires, 20 Rue des Minimes, Douai (Nord), France.

One important difficulty remains to be resolved, and that is the distinction between localized shadows due to active or inactive tuberculosis, and those due to the early stages of massive fibrosis (category A). Mann (1951) claimed to be able to distinguish these two types of radiological appearance, but many other observers have found difficulty in this differentiation, and we have found serious inter-observer error in the interpretation of these early localized shadows. Mention has already been made of the disagreement between the British and French independent readings in such cases. It is our present practice to read all localized shadows upon a background of category 2 or 3 simple pneumoconiosis as category A unless the appearances are quite characteristic of healed inactive tuberculosis, and this is the procedure that we recommend. Further investigation, especially by follow-up studies, will be necessary before this difficulty can be resolved.

Summary

As a first step towards solving the problem of the existing international disagreement concerning the classification of radiographs in pneumoconiosis an attempt was made to compare a classification used in the northern coalfields of France with that used by the Pneumoconiosis Research Unit in Great Britain, the latter classification being very similar to that proposed by the International Labour Office international conference on pneumoconiosis at Sydney in 1950.

A large number of films were read in consultation between British readers and French readers. As a result, a provisional joint classification was achieved. This classification was used on a further group of films, and after a second joint consultation a final agreed classification embodying the essential features of both systems was reached.

This classification is given in detail (Appendix 1). It is similar to the international classification (Appendix 2), but makes formal provision for the description of morphological types of simple pneumoconiosis.

At a meeting of mine medical officers and others at Douai in June, 1951, it was agreed to give the classification a trial in various centres in France, Belgium, and Holland.

To ensure the accurate use of this classification, standard films exemplifying the categories have been selected and are kept at Cardiff in Great Britain and at Douai in France. It is suggested that it will also be necessary to have a group of films which have been classified according to the agreed method which could be sent to other workers to be read by them to ensure that they are using the classification correctly.

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APPENDIX 1

PROPOSED ANGLO-FRENCH CLASSIFICATION OF RADIOGRAPHS IN PNEUMOCONIOSIS

The classification only concerns those common and well recognized kinds of pneumoconiosis that give rise to the appearance of bilateral, discrete, more or less circular opacities in radiographs of the chest, e.g. silicosis, coalworker's pneumoconiosis, etc.

At present, the classification is based solely on radiographic appearances such as may be seen in a full size postero-anterior or antero-posterior chest radiograph of a satisfactory technical standard taken in inspiration. It is not intended to define pathological entities, or to define stages of disease for compensation.

It is obvious that such a classification must be severely limited. It must be simple and flexible, and it must allow for the use of generally recognized symbols which may be easily codified. The proposed classification is based on previous classifications, particularly the French system of Eck and Hanaut, the British system of the Pneumoconiosis Research Unit, and the international system proposed at Sydney in February, 1950.

From the point of view of the radiographic diagnosis of pneumoconiosis, the system recognizes two main groups of appearance: first, normal and abnormal (not necessarily pneumoconiotic); and secondly, specific appearances of pneumoconiosis.

Normal or not Necessarily Pneumoconiotic Appearances

Normal but not necessarily pneumoconiotic appearances are indicated by the letters O and X. O indicates normal films without any sign of pneumoconiosis. X indicates films showing shadows which are usually symmetrical, linear or circular in form, which may suggest pneumoconiosis but which are more likely to be due to other pathological conditions.

Appearances of Pneumoconiosis

Two main subdivisions are distinguished. They are (I) simple pneumoconiosis (P.R.U.), or *images ombres fines* (French), or pneumoconiosis with discrete opacities (I.L.O.); (II) progressive massive fibrosis (P.R.U.), *ombres étendues* (French), pneumoconiosis with coalescent or massive shadows (I.L.O.).

Simple Pneumoconiosis.—These films are denoted by numerals 1, 2, and 3 indicating the profusion of the opacities. In the case of categories 2 and 3, the letters P, M, and N are added to indicate the dominant morphological type of the opacities.

1. Abnormal films characterized by the presence of a small number of minute, more or less circular, opacities extending over not more than half of the medial two-thirds of the lung fields.

2. More numerous opacities extending over more than half of the medial two-thirds of the lung fields, but which are sparse or absent in the lateral third.

3. Profuse opacities distributed through the whole of both lung fields including the outer third.

P (pinhead) denotes opacities ranging in size from the limit of visibility to 1·5 mm. in diameter giving rise to profuse and uniform granularity.

M (micronodular) denotes more or less circular opacities ranging in diameter from 1·5 to 3 mm.

N (nodular) denotes discrete, more or less circular opacities, larger than 3 mm. in diameter.

Examples of pinhead, micronodular, and nodular films are given in Fig. 4.

The categories of the classification will be indicated in the following way :—

1
2 P, 2 M, 2 N,
3 P, 3 M, 3 N,

The opacities in category 1 are too sparse to be categorized in the types P, M, and N.

Progressive Massive Fibrosis.—These films comprise two main groups: coalescent shadows are indicated by the letter A, and massive shadows (equivalent to the French *ombres pseudo-tumorales*) designated by letters B, C, and D.

A. Shadows occupying at least one anterior rib space, generally formed by the coalescence of more or less circular shadows more than 1·0 cm. in diameter with indefinite margins and of uneven density. Next to the letter A, one can add the small letters p, m, n, in order to indicate the dominant type of the radiological appearance upon which the lesions have developed. If the underlying appearance is impossible to describe, the letter A is followed by a "?".

Example: Ap, Am, A?.

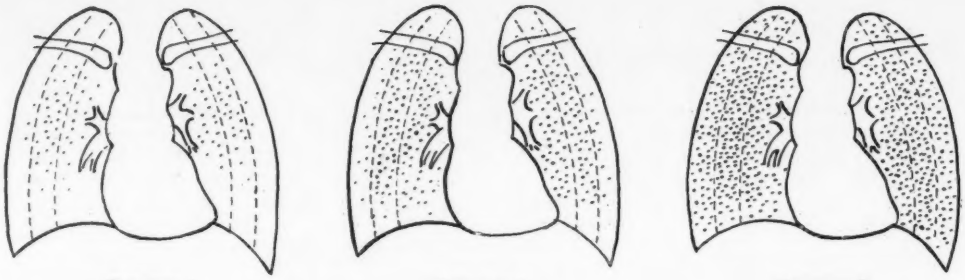
B. Dense shadows which are more extensive, better defined and of more homogeneous density which extend over less than three anterior rib spaces.

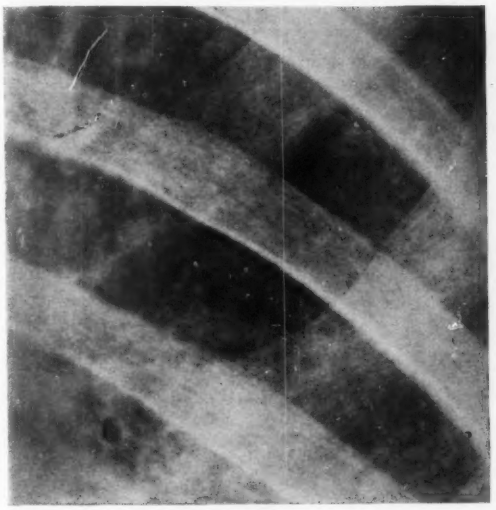
C. The same type of shadow extending over more than three anterior rib spaces.

D. The letter D indicates that one of the preceding class of shadows is associated with serious distortion of the pulmonary architecture.

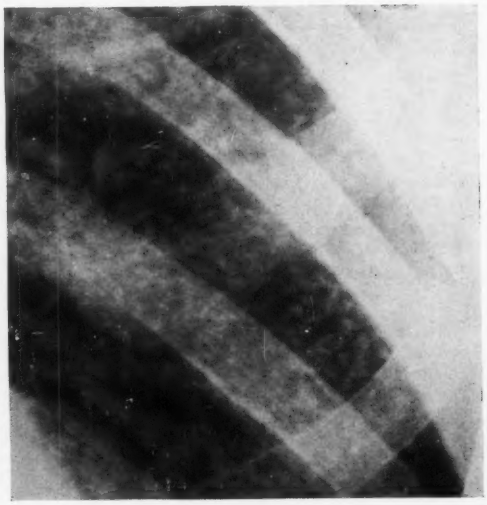
The classification only takes account of the predominant type of appearance. In cases of mixed appearance, the most advanced is codified, and when there is asymmetry, the most seriously affected side is codified.

This classification requires in addition to verbal descriptions, a set of standard films which has been established at Douai and at Cardiff.

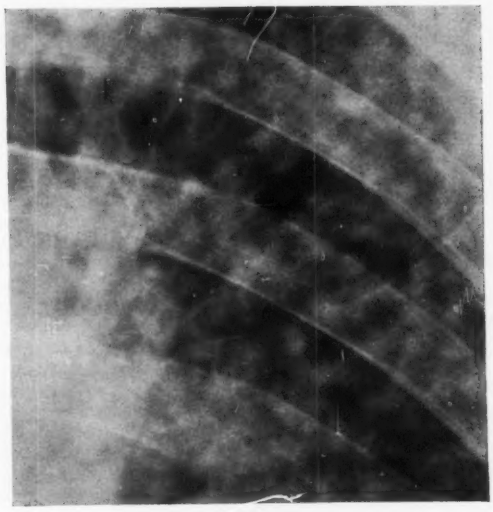




Pinhead



Micronodular



Nodular

FIG. 4.—Reproduction of the left mid zone of F. ach standard films illustrating pinhead, micronodular, and nodular types.

CODING OF THE ANGLO-FRENCH CLASSIFICATION

Appearances not due to pneumoconiosis *Images non pneumoconiotiques*		O X
Appearances of pneumoconiosis *Images pneumoconiotiques*	Simple pneumoconiosis, or *ombres fines*, or pneumoconiosis with discrete opacities	1 2 P, 2 M, 2 N 3 P, 3 M, 3 N
	Progressive massive fibrosis, or *ombres étendues*, or pneumoconiosis with coalescent or massive shadows	Ap, Am, An, A? B C D

APPENDIX 2

SUGGESTED INTERNATIONAL SCHEME FOR THE CLASSIFICATION OF RADIOGRAPHS* IN SOME OF THE PNEUMOCONIOSES

This classification is proposed for the purpose of promoting clarity and mutual understanding between scientists concerned with the study of pneumoconiosis. It has no relation to the legal definition of stages of pneumoconiosis for compensation.

Principles

The classification only concerns those common and well recognized kinds of pneumoconiosis that give rise to the appearance of bilateral, discrete, more or less circular opacities in radiographs of the chest, e.g. in silicosis, coalworker's pneumoconiosis, etc.

At present the classification is based solely on radiographic appearances such as may be seen in a full size P.A. or A.P. chest radiograph of a satisfactory technical standard. It is not intended to define pathological entities.

No interpretation other than pneumoconiosis is to be admitted; secondary conditions such as emphysema, pneumothorax, pneumonia, etc., are to be separately described if present.

No reference is to be made to such variations in radiographic appearances as may be seen in individuals without pneumoconiosis. All such appearances, in the absence of other diseases, are to be classified as "within normal limits". It is recognized that appearances such as have been described as "exaggeration of linear markings", "generalized arborization", etc., may be of clinical importance in certain industries, but their significance appears too uncertain for them to be included in a classification of radiographic appearances of pneumoconiosis.

Terms such as "initial", "terminal", "progressive", "infective" which suggest a definite process of development, or a definite pathogenesis, should not be used in describing a radiograph.

Descriptive terms applicable to various types of radiographic pattern such as "small or large mottling", "pinhead", "micronodular", "nodular", "cobweb", "angel wings", "*pseudotumorale*", etc., may have a colloquial descriptive value, but they are not necessary, and should not be included in the basic classification. In particular, the word "reticulation" should never be used.

The Classification

A major subdivision is recognized between films showing only small, more or less circular, discrete, disseminated opacities, and those showing coalescent or massive shadows. Although there is convenience in the phrases "simple pneumoconiosis" and "complicated pneumoconiosis" to describe these two major divisions, the simplicity of the one and the presence of any special complicating condition in the other are open to too much doubt to permit the use of these terms. Thus there are two major classes of films: (1) pneumoconiosis with discrete opacities; and (2) pneumoconiosis with coalescent or massive shadows.

Within each of these two major subdivisions it is necessary to have subdivisions or categories representing increasing degrees of abnormality.

In pneumoconiosis with discrete opacities three main categories are proposed. The inaccuracies of radiographic classification are too great to permit the use of a greater number. A fourth category is suggested for those cases in which the discrete opacities are of a character that does not enable them to be included in any of the three main categories.

These categories are to be referred to by the numbers 1, 2, and 3; the miscellaneous group is to be referred to as X.

In pneumoconiosis with coalescent or massive shadows the subdivisions are made on the basis of the extent and density of the coalescent or massive shadows. An extra subdivision is made for those cases in which gross distortion of the bronchial tree and pulmonary parenchyma has occurred. These subdivisions are to be referred to by the capital letters, A, B, C, and D. In these cases, it is unnecessary to refer to the category of the pneumoconiosis upon which massive fibrosis is superimposed.

* From the Report of the International Labour Organization's third international conference of experts on pneumoconiosis held in Sydney in 1950.

The limits of the categories are to be defined in two ways ; first by verbal definitions as given below ; and second by standard reference films (see notes below).

The classification proposed is the following :

Radiographs Within Normal Limits

Radiographs designated 0.

Pneumoconiosis With Discrete Opacities

Radiographs Designated 1.—In these radiographs a small number of opacities may be seen in at least two anterior rib spaces extending over not more than half of the medial two-thirds of the lung fields.

Radiographs Designated 2.—In these radiographs opacities extend over more than half of the medial two-thirds of the lung fields but are sparse or absent in the lateral third.

Radiographs Designated 3.—In these radiographs profuse opacities extend over the whole of both lung fields including the lateral third, although they may be sparse or absent above the clavicles.

Radiographs Designated X.—These are radiographs with discrete opacities whose appearance does not accord with any of the preceding categories.

In cases where there is an uneven distribution of the opacities in different areas of the lung fields, the category is determined by the most advanced abnormality that is present over at least half of a lung field.

Pneumoconiosis with Coalescent or Massive Shadows

Radiographs Designated A.—In these films opacities more than 1 cm. in diameter may be seen in one or more areas, commonly coalescing, but not constituting a massive shadow of even density.

Radiographs Designated B.—In these films one or more massive shadows are present, extending over less than the equivalent of three anterior rib spaces on either side.

Radiographs Designated C.—In these films large massive shadows of uniform density extend over the equivalent of three or more anterior rib spaces on either side.

Radiographs Designated D.—In these radiographs one or more massive shadows are present associated with gross distortion of the pulmonary anatomy. The massive shadows may of themselves be such as would be classified as A, B, or C in the absence of such distortion.

Notes

Radiographic technique should be of the highest standard. The penetration should be such that the outline of the vertebral column, but not the inter-vertebral discs, may be distinguished through the heart shadow.

Radiographs should be coded simply by giving the appropriate number and letter. Descriptive terms may be used at the convenience of individual observers to qualify any category. This allows for reference to the size of opacities if this is considered important : e.g. 2. " macronodulation " ; 2. " micronodulation " ; 3. " pinhead " ; 3. " nodular ".

In radiographs with coalescent or massive shadows the appropriate numbers for the associated discrete opacities may also be given in brackets : e.g. (2) B, (3) A, etc.

Additional interpretation may similarly be added : e.g. (3) A. pneumothorax R. lung.

To assist in consistent classification it is suggested that standard reference radiographs exemplifying the categories should be held by some central international organization such as the I.L.O. Good reproductions of these films should be made for distribution to those wishing to use the classification.

In addition, sets of radiographs derived from cases of the commoner kinds of pneumoconiosis might be classified according to the scheme by a committee of experts and be held by the same central organization. Observers in various countries might then check their use of the scheme by seeing if their classification of these films agree with that of the committee of experts.

Brit. J. industr. Med., 1951, **8**, 256.

PNEUMOCONIOSIS IN BOILER SCALERS

BY

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Every six months or so the majority of steam-driven ships spend a few days in docks having their boilers scaled and cleaned. In the larger docks there are men who are employed full time in this occupation, but elsewhere and in industry generally the cleaning is more often done as an occasional job. The total number of men engaged in the work full time is not large, but the occupation is a very dusty one and carries a definite risk of pneumoconiosis. Some details of the processes involved were given by Harding, McRae Tod, and McLaughlin (1944). Working in very confined spaces the boiler scaler crawls along with a lamp and a hammer chipping off the scale as he goes; frequently the boiler is still very warm, and he works in a hot atmosphere. The considerable amount of dust comes from two sources: that produced by breaking off the scale deposited in the tubes from the water, and the flue dust in the fire tubes arising from the coal or other fuel. Although the boiler scale contains varying quantities of silica this is present mainly as silicate, and it seems likely that the flue dust is the more important since it may contain free silica from the coal. Cooke (1930) reported 26·4% of silica in a sample of flue dust, Harding and others (1944) 6·1%, while in a sample taken recently in Hull we have found 10%.

Since the original case described by Cooke (1930), there have been only three further reports of necropsy findings: Williams (1931), and Harding and others (1944 and 1947), but the clinical and radiological findings have been reported on a number of cases, notably by Dunner (1943), and Dunner and Hermon (1944). In this report we give an account of eight boiler scalers whose lungs we have examined in whole or in part.

Case 1.—C. M., aged 60 years, had been employed as a marine boiler scaler for 44 years. He first attended his doctor in 1929 with "chronic bronchitis", and not again until 1946 when he was treated for six months for the same complaint. During this latter period he was referred to the tuberculosis centre where he was found to have a poor chest expansion and a diminished resonance over the left lung. The radiograph showed multiple small rounded nodules scattered diffusely throughout the left lung and in the upper and mid zones of the right lung. This nodulation was considered to be due to the second stage of silicosis. He again attended his doctor during three months in 1947 for treatment of his "bronchitis", and was advised to give up his occupation. He continued his work, however, until January, 1951, when he had an acute febrile respiratory illness from which he died.

A post-mortem examination was made on January 22, 1951, by one of us (A.P.M.). The body was wasted; the fingers showed slight clubbing. The mucous membranes of the trachea and bronchi were acutely inflamed, and a considerable amount of thick green mucopus was present in them. Old firm bilateral pleural adhesions were present.

The left lung was voluminous and showed a group of white fibrous plaques, approximately 1 cm. in diameter on the pleural surface of its mid-lateral aspect. A solid hard mass 3 cm. in diameter was palpable deep to these scars and lying in the upper lateral extremity of the lower lobe. Other tiny nodules were palpable deep to the pleura and scattered throughout the lung. On section the lung showed a heavy, diffuse, jet black pigmentation, and tarry black fluid exuded from the cut surface. Glistening black nodules 1 to 2 mm. in diameter, rounded or stellate, were scattered fairly uniformly throughout the lung and gave a gritty sensation to the knife. The majority of these nodules were surrounded by groups of small cysts 1 to 3 mm. in diameter giving the classical picture of "focal emphysema". A few larger cysts formed from coalescence measured up to 6 mm. in diameter. The large solid pigmented mass had broken down in its central portion to produce a cavity 13 × 7 × 7 mm.

The right lung was not quite as heavily pigmented as the left but a similar nodulation with focal emphysema was present throughout: it was more oedematous, and the lower lobe was partially consolidated by pneumonia, thick pus oozing from the terminal bronchioles. The hilar glands on both sides were enlarged, the left group more than the right, and all showed a heavy, diffuse, black pigmentation.

Slight atheromatous changes were present in the aorta and coronary vessels but the heart muscle and valves

FIG. 1.—Large unstained section (reduced) of left lung of Case 1: focal emphysema, pigmented nodulation.

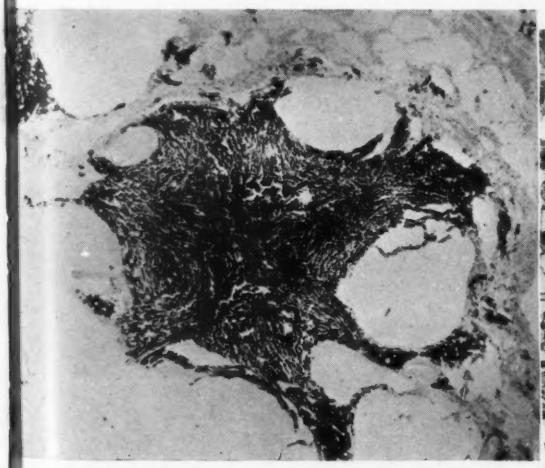


FIG. 2.—Pigmented nodule in Case 1 with radial fibrosis: focal emphysema. Haematoxylin and eosin. × 24.

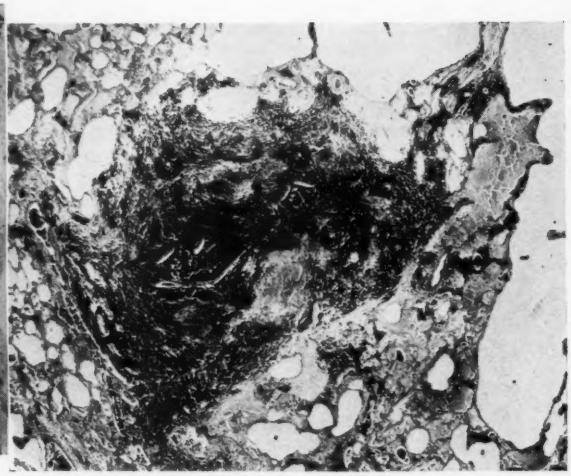


FIG. 3.—Early diffuse fibrosis in Case 1: focal emphysema. Haematoxylin and eosin × 12.

showed no marked abnormality apart from some hypertrophy of the right ventricle. The liver showed some passive venous congestion but all the other organs appeared to be normal.

Death was attributed to acute tracheo-bronchitis and bronchopneumonia accelerated by pneumoconiosis.

After fixation in formalin the lungs had a blue-black mottled pleura with a pattern of white lines. The cut surface of the lungs (Fig. 1) showed fairly marked focal emphysema and a diffuse, black, fine nodulation much of which was palpable.

Histological examination (Figs. 2, 3) showed small numbers of dust cells in alveoli and accumulations of black pigment in the perivascular, peribronchial, interlobular and subpleural lymphatics. Most of the pigment was, however, in larger nodular masses distributed fairly evenly throughout the lung. These had a roughly stellate outline and were bounded by emphysematous spaces that were separated by the projecting spinous processes of the nodule. Collagenous fibrosis was present in the nodules and in the perivascular and other aggregates. It was linear or radial and not whorled. Fibrosis was more prominent in the area of massive consolidation in the left lower lobe, the central portion of which had undergone colliquative necrosis. Much pigment and a moderate amount of linear fibrosis were present in hilar lymph nodes. No evidence of tuberculosis was seen.

Case 2.—G.C., aged 61 years, was employed as a marine boiler scaler by the same firm as Case 1 continuously for 30 years, beginning when a youth. During the last five years of this period he visited his doctor frequently, complaining of a productive cough and shortness of breath. His symptoms progressed until he was forced to give up his employment, and he subsequently received sick benefit and did no work for two and a half years. In 1942 he began work cleaning motor buses. This occupation he found sufficiently light and comparatively clean. When examined by the Mass Radiography Service in October, 1947, his general condition was found to be poor. Bronchial breath sounds were present throughout his chest and numerous moist râles were heard. The radiograph (Figs. 4, 5) showed " widespread reticulation that spared the apices ; both lobes of the diaphragm were flattened " : these appearances were interpreted as due to early pneumoconiosis. Another radiograph a year later was reported as showing generalized nodular appearances over the whole of the lower zones of both lungs and to a lesser extent in the right upper zone. The lung markings were almost entirely absent in the mid and lower zones, and there was obliteration of the right costophrenic angle. This combination of nodulation and absent lung markings was interpreted as indicating a fairly advanced stage of silicosis. He was referred to the tuberculosis officer for surveillance, but tubercle bacilli were not found in his sputum after many examinations. His general condition slowly deteriorated. He gradually lost weight, and died in January, 1951.

On January 15, 1951 a necropsy examination was made by one of us (A.P.M.). The body was emaciated. The mucous membranes of the trachea and bronchi showed chronic inflammation. Bilateral, old, firm pleural adhesions were present especially on the left side. The left lung showed a few white scars on its apical surface. It was rather voluminous and on section showed a heavy black pigmentation. Hard, tiny nodules that were just palpable were scattered fairly uniformly throughout the lung : these nodules were jet black and shiny and surrounded by small cystic cavities approximately 1 to 3 mm. in diameter. These areas of focal emphysema were more obvious in the lower lobe. The right lung showed a picture similar to the left, but the pigmentation was not as heavy and diffuse so that the nodular aggregation was more obvious. The lower lobe of this lung showed acute bronchopneumonia with purulent exudate in the bronchioles. The hilar lymph nodes were enlarged, and evenly and darkly black. No evidence of tuberculosis was found. There were advanced atheromatous changes and calcification of the aorta and coronary arteries. The cusps of the aortic valve were calcified, and there was some hypertrophy of each ventricle. The other organs showed no gross abnormality apart from venous congestion of the liver and atherosclerotic scars in the cortex of the kidneys. Death was attributed to acute bronchopneumonia, accelerated by pneumoconiosis and arteriosclerosis.

After fixation in formalin the lungs were very similar to those of Case 1 but the changes were not quite as marked.

Histological examination (Figs. 6, 7, 8) showed very few dust cells in the alveoli, most of the pigment lying in accumulations in the perivascular lymphatics where there was slight but definite collagenous fibrosis. There were many irregularly shaped nodules with a linear or radial arrangement of collagen fibres enclosing aggregations of pigment-filled cells. (This type of reaction we propose to call " mixed dust fibrosis " ; this term is discussed later in the paper.) These nodules varied in size up to nearly 1 cm.; round the majority of them there was well marked focal emphysema. Acute purulent bronchopneumonia was present in the right lower lobe. Much of the black pigment disappeared on incineration, but there was an appreciable residue of iron oxide : acid treated incinerated sections showed a fine dusting with silica in the nodules.

Case 3.—W.P., aged 64 years, had been a ship's boiler scaler all his working life, over 40 years. He cleaned mainly the Scottish marine type of boilers with the combustion chamber running through the boiler. He worked inside the boilers. For some five to six years before his death he suffered from " chest trouble ", and ceased work because of disability in 1946. He made no claim for compensation, and was therefore not seen by the Pneumoconiosis Medical Panel during life. He died in 1951 from congestive heart failure due to pneumoconiosis, emphysema, and chronic bronchitis.

After fixation in formalin the lungs had a blue-black pleura in which were non-palpable white lines and white plaques up to 2 cm. in diameter. The cut surfaces were very black and had numerous hard black nodules that were round or stellate and mainly 1 to 2 mm. diameter.

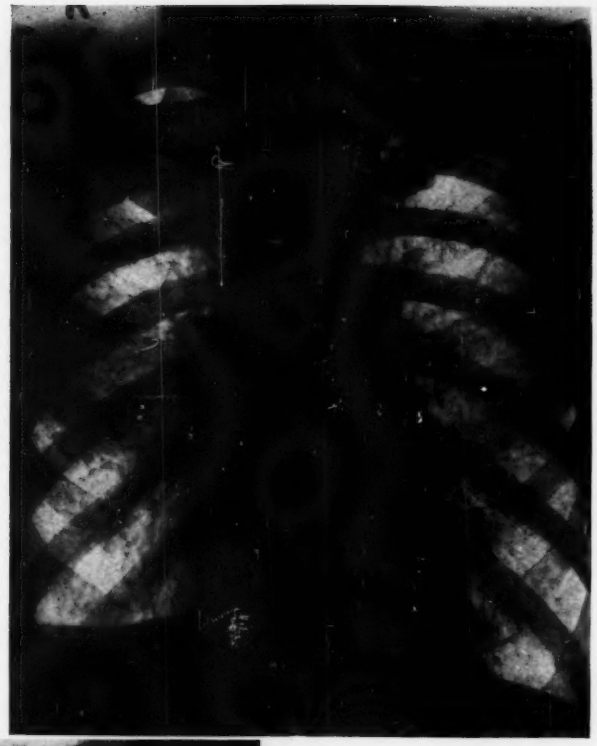


FIG. 4.—Radiograph of Case 2 (reduced).

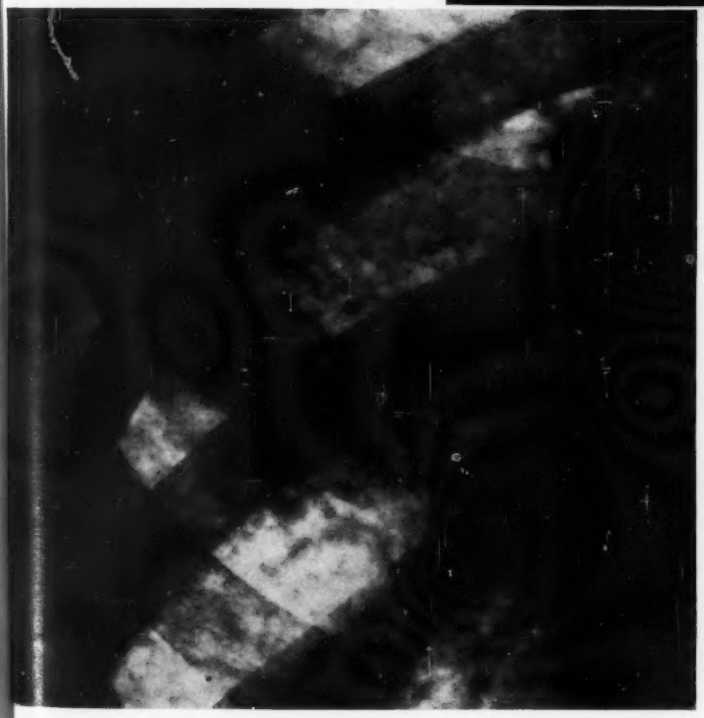
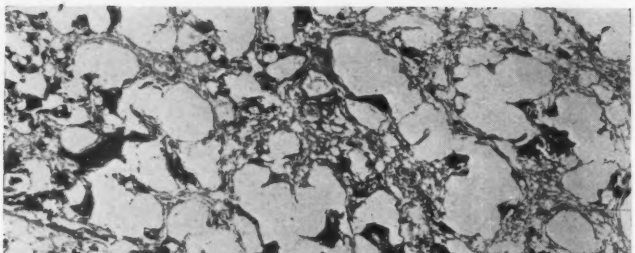
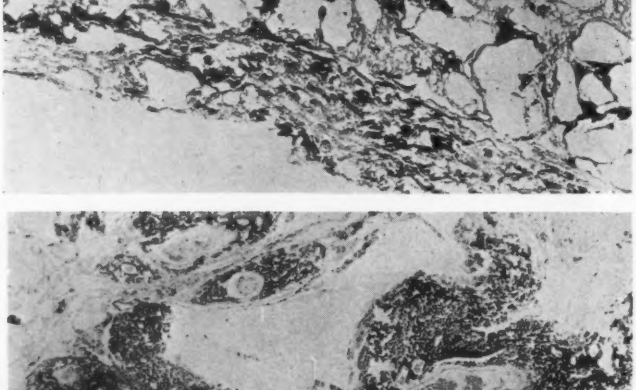
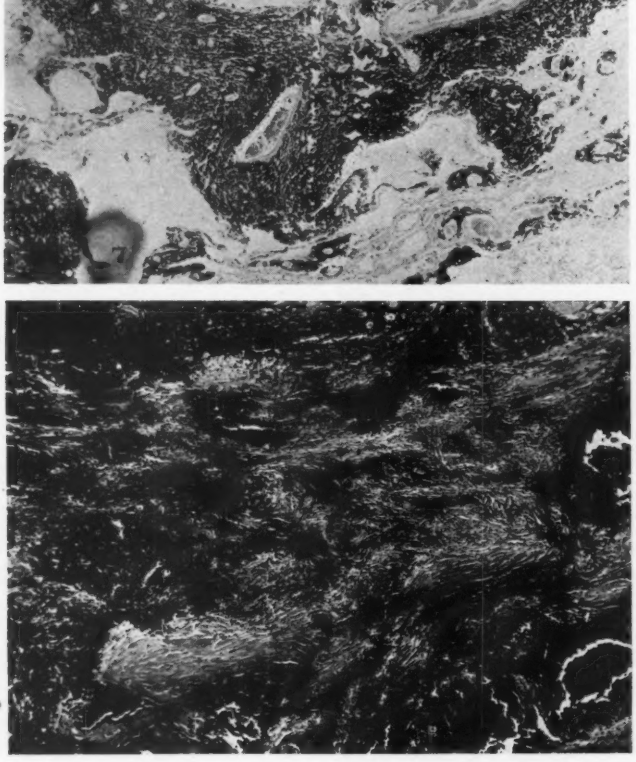


FIG. 5.—Area from Fig. 4 (natural size) showing fine nodulation.







There was marked focal emphysema as well as marginal and apical bullous emphysema. The hilar lymph nodes were very large, black and firm.

Sections (Figs. 9, 10) were similar to those in the preceding cases but collagenous fibrosis was more conspicuous in the nodules and in places resembled early silicotic nodulation. No evidence of tuberculosis was found on naked eye or microscopic examination.

Case 4.—R.M., aged 64 years, had been a ship's boiler scaler in the Liverpool area practically all his working life and certainly for more than 30 years. From May, 1939, he worked only on and off, and in May, 1945, he gave up work entirely "because of his chest". He died in May, 1951, and a post-mortem examination was made by Dr. R. C. Nairn who gave the cause of death as "emphysema and chronic bronchitis; anthracosis; myocardial degeneration".

The lungs, which had been fixed in formalin before we received them, were very torn and had evidently been grossly adherent to the chest wall. There was dense hyaline thickening of the pleura over the back and sides of both upper lobes. The lungs were very black and showed marked marginal and focal emphysema. Hard, glistening, black nodules of irregular shape up to $\frac{3}{4}$ in. in diameter were present in the apical and subapical regions of both lungs. Similar nodules were scattered throughout the lungs but were progressively smaller and fewer from the apices to the bases. Below the right apex was a ragged area that appeared to result from necrosis in an area of massive fibrosis, but might have been due to tearing at necropsy. The hilar nodes were not very large; they were very black but not very hard. Microscopically there was marked "mixed dust fibrosis" with moderately marked focal emphysema. The larger areas of fibrosis showed central necrosis. In these larger areas of fibrosis staining of the elastica revealed many solid arteries that were not readily distinguishable

FIG. 6.—Focal emphysema in Case 2: mixed dust fibrosis. Haematoxylin and eosin × 4.

FIG. 7.—Perivascular mixed dust fibrosis in Case 2. Haematoxylin and eosin × 12.

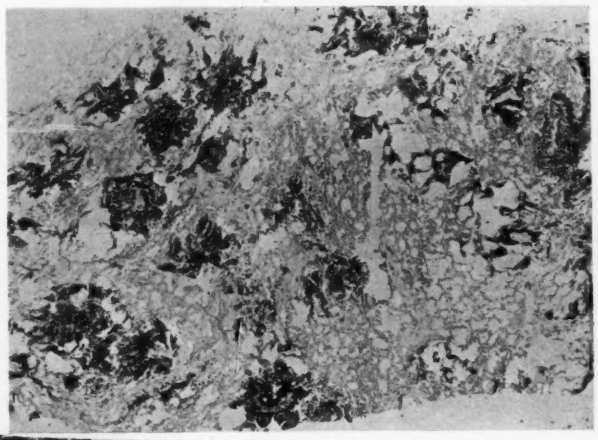
FIG. 8.—Diffuse fibrosis in Case 2 of mixed dust type: pigmentation. Haematoxylin and eosin × 12.

with other stains. Nothing at all suggestive of tuberculosis was found, and it seems probable that the necrosis resulted from ischaemia.

Case 5.—J.W.L., aged 47 years, had been employed as a marine boiler scaler for 30 years. Except for a slight cough he had been well until February, 1946, when he complained of epigastric pains, anorexia, and flatulence. He was investigated in March, 1946, and a radiograph of his chest showed an opacity in the region of the right base, that was subsequently diagnosed as a bronchogenic carcinoma. His general condition gradually deteriorated with loss of weight and distressed breathing, and he died with multiple secondaries in January, 1947. The radiograph of his chest did not suggest pneumoconiosis.

A post-mortem examination on January 31, 1947, showed many secondary nodules in the skin of the abdomen and back, the largest the size of a walnut. The left lung showed a blue-black mottling of its pleura and several old adhesions. A generalized fine emphysema was present with some bullae at the anterior margin. Apart from the anterior margin the lung showed an almost uniform black pigmentation but some rather indefinite small nodules were palpable. The right lung in its upper portion showed a similar picture to the left, but nodules were more readily palpable. A carcinoma was present in the lower lobe extending half-way across it from the hilum. The remainder of the lower lobe appeared black with grey markings and felt hard, though not as hard as the areas of massive fibrosis in the lung of a miner. The pleura showed marked fibrous thickening over the whole lung. The hilar lymph nodes were moderately enlarged, black and very firm. The bronchial carcinoma had invaded the pericardium and heart muscle. The right ventricle of the heart was hypertrophied. Generalized metastases were found in the abdominal viscera and in two ribs.

Histological examination of the lungs showed a good deal of black pigment in dust cells in the alveoli, in the alveolar walls, and in the subpleural lymphatics. Focal accumulations were present in the perivascular lymphatics and in some of these there was a slight reactive fibrosis around the pigment. A few emphysematous cysts were present, but "focal emphysema" was not a marked feature. There was rather more fibrosis in the right lower lobe with much included pigment, but the lung here appeared to be compressed by the growth rather than grossly fibrotic. The tumour had the structure of a poorly differentiated squamous cell carcinoma. The hilar lymph nodes showed a fairly well marked "mixed dust fibrosis", but no whorled nodules were present. Incinerated sections revealed only moderate amounts of iron and a slightly larger residue of silica than is found in sections from the lungs of men having no unusual exposure to dust.



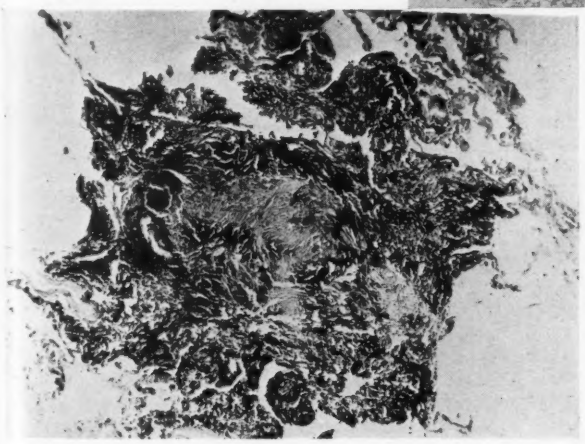


FIG. 9.—Mixed dust fibrosis in Case 3: focal emphysema: oedema. Haematoxylin and eosin × 4.

FIG. 10.—Nodule of mixed dust fibrosis in Case 3 with considerable collagen formation. Haematoxylin and eosin × 24.

Case 6.—W. McD., aged 60 years, had been in regular employment as a ship's boiler scaler for 25 years in the Lancashire area. His occupation before the age of 25 is unknown to us. In 1940 he had to give up work on account of disability from valvular disease of the heart. He was subsequently largely confined to bed, and died in June, 1949. After a post-mortem examination by Dr. Carraher, of Warrington, the cause of death was given as heart failure due to mitral stenosis.

The lungs after fixation in formalin showed slight thickening of the blue-black pleura in which were some white lines: a few old adhesions were present. Many small, black non-palpable nodules surrounded by focal emphysema were present in the lungs. The hilar lymph nodes were moderately enlarged, very black, and moderately firm.

Histological examination showed well-marked mixed dust fibrosis with moderate focal emphysema: no silicotic nodules and no evidence of tuberculosis were found. The hilar lymph nodes were very pigmented, and showed marked linear fibrosis but no whorled nodules. Incinerated sections showed much iron in the nodules.

Case 7.—H. B., aged 57 years, had been employed for 17 years as a boiler scaler at a large industrial works in Lancashire. His other employment is unknown, but is believed not to have involved exposure to dust. He began to complain of dyspnoea in 1941, and died in March, 1948. After a post-mortem examination by Dr. A. McNeilly, of St. Helens, the cause of death was given as carcinoma of the left lung with secondary growths in both lungs.

The lungs had been fixed in formalin when seen by us. The left lung had evidently been densely adherent to the chest wall from which it had been torn and cut. A firm white tumour 1½ in. in diameter was present at and above the hilum and surrounding the main upper lobe bronchus: secondary nodules up to 2 mm. in diameter were present throughout the lung which was not heavily pigmented and which contained no definitely fibrous nodules. The right lung showed a thickened pleura with denser scars near the apex and some old adhesions. Small nodules of new growth were scattered throughout. The lung was not very pigmented and no fibrous nodules were seen. The enlarged hilar lymph nodes were black, of normal consistency, and contained creamy nodules of tumour.

Histological examination showed an undifferentiated bronchial carcinoma in all sections, and considerable oedema of the lung. There was a moderate amount of black pigment around the pulmonary vessels, and a slight increase in reticulin fibrils around and among the aggregates of pigment, but no collagenous fibrosis. No evidence was found of tuberculosis nor was anything resembling silicotic nodulation seen.

Case 8.—J. F. was 48 when he died in 1949. From 1913 to 1919 he was employed as a doffer and warehouseman in a woollen mill; from 1919 to 1941 boiler fireman on a Lancashire boiler in a woollen mill; from 1941 to 1946 engine man in charge of the engine room at same firm. From 1919 to 1946 he also cleaned and scaled the boiler once a month and the economizer every two months. An analysis of the flue dust showed 33% total silica and 4% free silica.

He fell ill in August, 1946, and in September of that year was admitted to the General Infirmary at Leeds under Dr. H. H. Moll who made a diagnosis of silico-tuberculosis. He was transferred to a sanatorium where he stayed until April, 1948. During this period his sputum consistently contained tubercle bacilli. Radiographs of his chest showed a large cavity in the region of the right apex with reticulation and a diffuse mottling and nodulation in the lung fields generally. The nodulation was most clearly defined in the last of the series. There was disagreement among the specialists consulted as to whether the appearances were due solely to tuberculosis or to silico-tuberculosis.

A post-mortem examination was made by Dr. H. H. Smith, of the Forensic Medicine Department, Leeds University, on April, 8 1949. "There were dense pleural adhesions covering the whole surfaces of both lungs. These were especially dense at the apices of both lungs and on the posterior surface of the right upper lobe. The lungs both felt nodular, the size of the nodules being up to a diameter of ½ mm. Especially in the apices of both lungs there were old and active areas of tuberculosis. Also scattered through the lung substance and in relation with the nodules the lungs presented an anthracotic silicotic appearance with a superadded caseous and purulent tuberculosis. Microscopical frozen sections of the lung showed numerous areas of anthra-

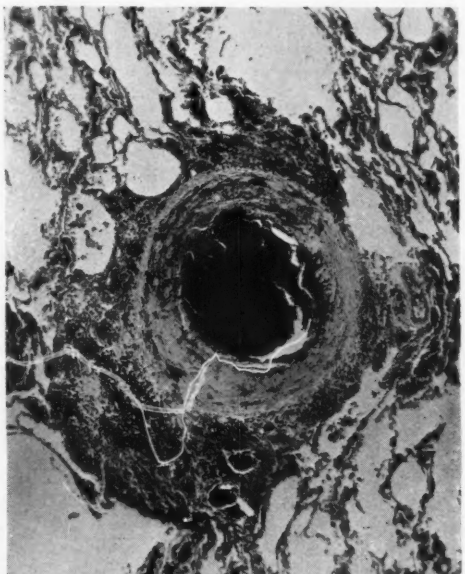


FIG. 11.—Nodule of healed tuberculosis with central calcified area in Case 8. Haematoxylin and eosin × 24.

cosis together with silicotic nodules surrounded by a dense fibrous capsule". The cause of death was given as "congestive heart failure following pulmonary tuberculosis and anthracotic silicosis". On the strength of this necropsy report and the diagnosis of Dr. Moll, the widow was successful in her claim for compensation.

The only material available to us was a single paraffin block of lung. Sections from this showed several nodules about 2 mm. in diameter with a thick, dense collagenous outer zone enclosing necrotic, partially calcified material (Fig. 11). In our opinion these nodules are healed tubercles, but there is insufficient evidence for us to decide that silica played no part in their production. The rest of the section showed only slight mixed dust fibrosis.

Discussion

The first four of these eight cases had pneumoconiosis of sufficient severity to produce disability and to be a factor in the cause of death. Cases 5 and 6 had definite pneumoconiosis but of lesser degree and probably playing little part in their deaths. Case 7 had a negligible amount of pneumoconiosis, while in Case 8 we consider the presence of pneumoconiosis unproven by the inadequate pathological examination although it was accepted by H.M. Coroner and by a court of law deciding compensation. These men had been employed as boiler scalers for 44, 30, 40, 30+, 30, 25, 17, and 27 years respectively, the first seven continuously, but the last only about once a month. The extent of the pneumoconiosis thus corresponded fairly well with the length of employment. In the absence of tuberculosis disability was not produced by less than 30 years' exposure.

Only one of the eight had tuberculosis (Case 8). Two of them (and one of the four cases previously reported) had bronchial carcinoma. These numbers are too small for any conclusion to be drawn from them. Three of them died of bronchopneumonia: in this connexion it may be relevant that Channell (1945) noticed a high incidence of upper respiratory infections in naval boiler scalers.

The type of pneumoconiosis that commonly occurs in boiler scalers appears essentially similar to that found in S. Wales coal workers (Gough, 1940, 1947). The deposition of dust is predominantly focal within small nodules distributed fairly evenly through the lungs mainly in relation to perivascular, peribronchial, interlobular, and subpleural lymphatics. In and around these deposits there is collagenous fibrosis not usually of severe degree and commonly linear or radial and not whorled. This type of reaction is often described as "dust reticulation", but we prefer the term "mixed dust fibrosis". It is in our experience a very common type of reaction found in many industries and trades where there is exposure to considerable quantities of dusts that vary considerably one from another, but all contain carbon and silica and usually iron oxide. In one sense it is a non-specific type of reaction (Heppleston, 1947), but we prefer to consider it as a form of modified silicosis until definite disproof of this view is given.

Although uncommon, whorled silicotic nodules may occur (Harding and others, 1944) just as they may occur in the lungs of a coal miner. Again as in other workers exposed to considerable quantities of mixed dusts, areas of massive fibrosis may occur as an extension of the process, and when they become large these areas may undergo necrosis in their central portions. Massive fibrosis was demonstrated radiologically by Dunner (1943), and was present in the first and fourth cases of this series. We are unconvinced by the argument that such lesions are invariably and necessarily due to added tuberculosis, and we found no evidence for such infection in our cases. On the other hand, we accept as a reasonable working hypothesis that local respiratory infections, tuberculous or other, play a part in their development.

Focal emphysema related to the nodules is a common feature of the pneumoconiosis of boiler scalers, and appears to increase with the length of employment. (We might here point out that the lungs in our cases were all cut before fixation, and were not first distended with formalin. Had they been treated by the methods of Gough, the focal emphysema would doubtless have been more conspicuous.) Focal emphysema of severe degree is most frequently seen in coal workers, but it occurs as a feature of the pneumoconiosis in many industries and trades where there is exposure to considerable quantities of mixed dust. We agree with Gough (1940) that it probably plays a large part in the production of dyspnoea and disability in these men. Williams (1944) suggested that it was produced by stenosis of respiratory bronchi as they pass through the coal foci, and Heppleston (1947) attributed it to the mechanical stress on the alveoli surrounding the nodules. We are inclined to believe that no single factor is responsible for its production but that it occurs only when considerable quantities of dust are present, and we have not yet seen it when the dust contained no free silica.

Although the number of men employed is small, we consider that there is now sufficient evidence for the inclusion of boiler scaling in the official schedule of occupations recognized as involving a risk of pneumoconiosis.

Summary

Pneumoconiosis in boiler scalers is essentially similar to that found in coal workers. In the

absence of respiratory infection the condition becomes sufficiently severe to produce disability only after about 30 years' exposure.

We are indebted to Dr. J. Egan for Cases 3 and 4; to Dr. D. L. McRae Tod for details about Case 5; to Drs. C. L. Sutherland and F. N. R. Price for Cases 6 and 7; to Dr. W. D. Buchanan for drawing our attention to Case 8 and for other help; and to Professor C. J. Polson for the necropsy report and for sections of the lung of Case 8. The large section of the lungs of Case 1 was made by Professor J. Gough; the photomicrographs were made by Mr. A. W. Collins, F.I.M.L.T.

Part of the expenses of this investigation were met by a grant to one of us from the Research Fund of Sheffield University.

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THE HAZARDS OF ROPE MAKING

BY

JAMES A. SMILEY

From Belfast Ropeworks Ltd.

The first rope makers to leave concrete evidence of their work were the Egyptians. We know from contemporary relics that about 3000 B.C. sails for ships in the Mediterranean Sea were rigged with rope which had to be spliced and run smoothly through cleats. One of the earliest representations of actual rope making is on a tomb of the Fifth Dynasty at Thebes, which shows a man and a boy with the inscription: "Twisting ropes of boat building". There are numerous references to ropes and rope making in classical literature in the works of Homer, Herodotus, Pliny, and others, and at least three references to spinning and to thread can be found in the books of Genesis and Exodus. A more modern author, Longfellow, in his poem "The Rope Makers" has given a graphic description of the ropewalk, a picture of processes which are much the same to this day. Indeed many of our workers who served during the late war in the East, and in particular one rope maker who watched the primitive methods of peasants in Cyprus, recognized the fundamental identity of the method of manufacture.

Preparation and Spinning

A modern rope works produces not only ropes with circumferences varying from $\frac{1}{2}$ in. to 28 in., but also threads, twines, and cords of an infinite variety. It has been estimated that this rope works has manufactured over half a million different types of products including ropes for mountaineering, cords for reins, lines for anglers, ropes for gallows, cords for the drums of regimental bands, log-lines, ropes for whale harpooning, plaited cords for window blinds, binder-twine for harvesters, and a host of other products.

In Great Britain over 1,500 tons of raw materials, mostly hemp, are used each week by rope works. The materials come from all over the world: the hard fibres of Manila hemp from the Philippines and Borneo, the New Zealand hemp from St. Helena, and Sisal hemp from East Africa and Sumatra all with different qualities, but all with fibres up to 10 ft. long. These fibres are used in the manufacture of strong heavy ropes and cables. The soft fibres of hemp and jute come mainly from Italy, India, and Chile, and are used in the main for the making of twines and cords. Some of these fibres average 8 to 9 feet in length. Flax is also used where strength and lightness of weight are required at the same time, and in recent years artificial fibres such as fibro and nylon have been increasingly used. The fibres come in bales weighing 250 to 300 lb., and these are stacked in bays up to 15 ft. high. Until modern lifting gear became available, accidents, often very severe, were common. Occasionally serious crushing accidents, or more rarely fractures of the legs, still occur, but these are being gradually eliminated. The bales are composed of bundles or "heads" which have to be separated by hand before the mechanical process begins. The separation of these "heads" stirs up an enormous quantity of dust. In the case of Indian hemp it was estimated some years ago that the loss of weight per bale was about 22 lb., almost 10%. Not all of this dust is vegetable. Indeed, on analysis, most of it was found to be soil and sand.

When hemp is harvested, the Indian peasant pulls the ripened plant, and ties each handful into a "head" by knotting it into a fairly tight loop at the end. He is paid by the number of "heads" he harvests. The "heads" are then retted in water, and after that they are laid out to dry before baling is done. As water is scarce, the retting tanks soon have insufficient water and become muddy. The mud adheres to the fibres when they are drying, and this, of course, increases the weight and bulk of the bale. There are two ways of dealing with the knotted heads. Either the head can be cut off, involving the loss of a substantial weight of raw material, and, what is more important, the shortening of the length of fibre, or the hemp could be harvested without being tied in bundles. This latter method would have had many advantages. In 1938 this method was the subject of a correspondence with the Board of Trade, the India

FIG. 1.—The woman on the left is teasing fibre which is being thrown on the " card " by the woman on the right. The jobs are interchangeable. Note the knife hanging from the waist, used for opening bales ; also dust deposits on the sides of the machine and hoods of extraction plant.

Office, and our local agents in India, but although a better price was offered for unknotted hemp, it was impossible to effect a change in the harvesting methods which have been carried on from prehistoric times. Thus the control of this dust hazard involves not only the usual methods of suppression and extraction, but the institution of a good system of irrigation, and a modification of traditional harvesting methods in a country thousands of miles away.

After the hemp has been unpacked and loosened, it is fed to machines which have two sets of chains fitted with bars carrying steel pins known as " hackle pins " (Fig. 1). The first chain carries the fibre to the second which, as it is travelling faster, has the effect of combing and straightening out the fibre, cleaning it, and forming it into continuous ribbons or " slivers ". A similar process is repeated several times, and the fibre is then drawn and finally twisted into yarn on spinning machines which also wind the yarn on bobbins ready for the making-up departments.

Respiratory Hazard

In the preparing room where the initial processes are carried out an immense amount of dust can be generated. In the recent past about one in 10 of all workers, mostly women, who worked in this room could expect within 30 years to develop a condition which was known to them as " pousse ", a degraded derivative of the French word meaning " dust ". (The linen and textiles trades were introduced to Ireland by the Hugenots.) The condition when fully developed seems to differ in no way from chronic bronchitis with emphysema. On taking up employment as a youngster, coughing on entering the dusty atmosphere is usual. Soon the worker seems to develop a tolerance, and the cough ceases. Occasionally, a young person within a week not only coughs but develops a " streaming cold ", and the eyes as well as the nose are affected. (This is a familial trade, and there are many examples of three generations of a family working side by side.) A tradition has grown up amongst the workers that such a young person should leave immediately, as she is liable eventually to develop " pousse ".

Further symptoms seldom develop under the age of 55 years. Cough in those affected then begins with the production of thick, tenacious mucus, and after a bout the patient is sufficiently dyspnoeic to simulate an attack of asthma. The victims usually feel better during the summer months and often at the weekend, but with the onset of cold weather or a return to the dusty atmosphere symptoms are exacerbated. In the

course of years, cyanosis gradually develops, and with it is associated polycythaemia. Wheezing is common but loss of weight in these women, most of whom are stout, is not as marked as might be expected, presumably because their dyspnoea enforces rest. Examination usually reveals the large, barrel-shaped thorax which heaves upwards but does not expand on inspiration. Vocal fremitus is diminished and the percussion note is hyper-resonant. In well marked cases it is sometimes impossible to hear the breath sounds because of the coarse sibilant rhonchi. The radiographic appearances are those of pulmonary emphysema. Pousse clinically seems to resemble bysinnosis as described by Fletcher (1949) and Schilling (1950). And like bysinnosis it develops only in those who work in the preparing and carding rooms and seldom or never in those involved in subsequent processes.

Dust control in the preparing and carding rooms of a rope works is very difficult, not only because of the vast amount of dust generated from the great mass of fibres passing at any one time through the carding machines, but because of the size and structure of the machine itself. Some success is being achieved by spraying the bales with water as these are opened, and later by treating the fibres with mineral oil as they pass through the "card". As will be seen from Fig. 1 dust extraction methods are also used, but it is difficult with the present machines to apply suction at all the points of origin of dust. The carding machines are now being re-designed.

Skin Hazards

In the manufacture of cordage, skin lesions are not uncommon. Ropes which are exposed to water and the weather must be treated with preservatives, and ropes and twines used in agriculture must be protected from insects. Those most commonly used are tar and its derivatives which are applied at an early stage with the result that workers in every section of the industry are exposed. Tar-oil is used to suppress dust in the preparing room, and thus serves a dual purpose. Occasionally some 20 workers out of some hundreds exposed will report within a few days with an acute erythematous rash of the forearm which may within a few days develop into a papular vesicular eruption. Usually the left forearm over which the impregnated sliver passes is the site affected, but sometimes the legs are also affected. The skin is intensely red, feels hot, is swollen, and on light pressure takes an impression of the finger prints. Severe itching is the rule. These outbreaks are sometimes, but not invariably, associated with the use of a fresh batch of the tar-oil, and occur most commonly not amongst the blondes or brunettes, but amongst sandy-haired workers. The offending batch is withdrawn, and the patients are transferred to other jobs and recover in a few days. Ordinary chemical analysis of dozens of batches has so far failed to reveal anything which can be incriminated as the cause. Calcium oxalate is a natural constituent of all the hard fibres, and occurs in varying amount in crystalline form. An investigation is at present being planned to determine if these outbreaks of acute dermatitis are related to the oxalate content of the raw material.

Oil folliculitis due to the use of mineral oils was formerly very common, and occurred at all stages of manufacture except spinning where the operator has little contact with the treated fibre. The forearms and the outer sides of the lower legs are

FIG. 2.—Receiving and coiling the slivers.

usually affected, as these are the parts mostly in contact with the masses of treated slivers (Fig. 2). The condition was so common that it was usually disregarded in the early stages. Now it is reported early by the fortunately increasing number of girls who are sensitive about their appearance. The condition is well controlled by the provision of facilities for good personal hygiene, by the supply of barrier creams, and if the lesions are established, by the transfer of the affected worker from further exposure until a cure is effected. In days gone by, workers had discovered for themselves that castor oil was useful in preventing these lesions, and they brought their own supply. For 12 years they have been supplied with sulphonated castor oil to apply when cleansing, and the problem is now only minimal

Amongst older women who have worked for years and have accepted the lesions as inevitable, hyperkeratosis occasionally develops. Of the 23 who have come to our notice in 13 years, two have developed malignant changes. The first had a small growth at the site of a hyperkeratotic plaque which on section proved to be a squamous celled epithelioma. Although she gave up her employment, she subsequently developed four other epitheliomata at similar sites on the left forearm during the following four years. The second was a younger woman of 46 whose exposure was slight, but in whom hyperkeratosis was extensive and severe. She also developed an epitheliomatous lesion but further inquiry revealed another possible cause, as her family doctor had been prescribing regularly a mixture of bromides and liq. arsenicalis for more than 20 years.

About 12 men work in the tarring shed. Here boiling tar is decanted into a large metal cylinder. Inside the cylinder is a heavy wire mesh cage into which are placed nets and ropes for treatment. After the materials have been thoroughly impregnated, the tar is allowed to escape into a closed tank and the cage within the cylinder is set in motion. Centrifugal force drives the surplus tar through the meshes into the cylinder, and it drains into the tank. The materials are then hauled out of the cage by lifting gear and transported to the finished product store for packing. The job is unpleasant and dirty and requires no skill. Consequently the turnover of labour is high. This is probably the reason that in 13 years no cases of tar warts or cancers have been seen.

Deafness

Plaiting is carried out by automatic machines which perform a series of complicated eccentric movements with cog wheels. As a result the plaiting room is very noisy. The noise is even more intense than that to which a boiler maker is exposed, being of the order of 150 to 200 decibels. The pitch of the note is even higher and more continuous. Fortunately only about 12 workers out of a total labour force of over 3,000 are required to attend the machines in this room. Without exception the older workers have extreme nerve deafness as a result of working in this room, and their condition differs in no way from boiler makers' deafness. Of recent years, replacements of older workers retiring or dying have been recruited only from those already deaf. In the meantime the engineers have been trying to produce a machine which will do the work noiselessly. Because the older workers are already stone deaf and because of our method of recruiting replacements, we have not supplied noise suppressors or such appliances for personal use.

Accidents

Spinning in the manufacture of cordage in no way differs in principle from textile spinning except that the bobbins are as a rule much larger. Contusions of the fingers and hands, often severe enough to cause fractures, are caused by the swiftly moving flyers. Partial or complete amputations are not infrequently caused by a loop of fine yarn encircling a finger or fingers and tightening rapidly and forcibly. Friction burns are caused by swiftly moving spun yarns and occasionally foreign bodies are driven into fingers. The dropping of heavy bobbins both in the spinning room and in transportation results in many fractured toes. A major problem in the reduction of the accident rate is to persuade girls to use suitably protected footwear, even when this is provided. Incised wounds are frequent, and are caused by the knives used to cut out the strands when the bank of bobbins is full. This type of accident also occurs in the preparing room when bales are being opened (Fig. 1). Scarcely a year passes without a hibernating snake being revealed when the bales are opened in this room. No injuries from this cause have occurred, but there is always a noticeable fall in the rate of work for a few days after such an incident !

The actual making or laying of the ropes may take place in the ropewalk which is over 400 yards long, or it may be done by machinery. The ropewalk is used nowadays only for the " laying " of heavy cables. The process is designed to lay three or more strands in apposition so that the natural tendency of each strand to untwist is counteracted by the tendency of its neighbour to untwist in the opposite direction. No specific hazard occurs here so no description need be given. Longfellow's description is more graphic than we could attempt and is substantially accurate even today.

FIG. 3.—Braiders at work.

Tenosynovitis

One of the important products of a rope works is netting, and although simple nets like tennis nets are made, the great bulk of netting is for fishing. The origin of the word net is obscure, but it is said to be related to " knit " or to " neat ", for a good net, with all the holes of the same size and shape, is neat. Whatever the derivation, the characteristic of a good net is that the meshes be equal in size and shape and that the knots be tied securely. Attempts have been made since the eighteenth century to invent a machine which could mechanize the process, but success has been only partial. In 1802 the French Government offered a reward of 10,000 francs for a machine to do automatic netting. Jaquard submitted a model, and was summoned to Paris by Napoleon who asked : " Are you the man who pretends to do what God Almighty cannot do—tie a knot in a stretched string ? "

A satisfactory machine is now in operation which can make nets rectangular in shape, but the greatest bulk of netting required is not rectangular, and the tailoring of these rectangles to the required shape and size has proved unsatisfactory. As a result about 300 women and girls are still engaged in the ancient craft of braiding. While they work conversation is impossible, as the shape of the net is determined by the number of meshes which each worker must count as she braids. It is impressive to enter a braiding room and see some hundreds of women standing or sitting, facing the wall and working in complete silence. As the net lengthens, in order to maintain tension, the braider sits on a stool, but after further lengthening requires the rearrangement of the net on the steel bar so that the braider is alternately standing or squatting on the stool all day long (Fig. 3). The speed at which braiding is done by experienced workers is very great and varies to some extent according to the material used, but 50 to 70 meshes per minute is not an uncommon rate. The dexterity gained in a series of complicated actions of flexion, extension, pronation, and supination at the wrist joint together with flexion and extension of the fingers, must be seen to be believed. As a result tenosynovitis, or peritendinitis crepitans as Thompson, Plewes, and Shaw (1951) prefer to call it, is common and may be regarded as the occupational hazard of the braider.

The condition seldom or never develops in the trainee worker because speed and efficiency develop together rather slowly. Those affected are women of experience, who for domestic or other reasons have left the industry for a time, and returning, attempt to achieve their former speeds. There is also an increase in the incidence of the condition beginning three to five days after the summer holiday. Here the younger workers are just as susceptible as the older. The hand which holds the needle is the one always affected. Almost any of the extensor tendons may be involved, but those most commonly felt are the brachioradialis (supinator longus), the abductor pollicis longus, the extensor pollicis brevis, and the radial extensors at the wrist.

From January, 1949, until December, 1950, 63 cases were seen, and on only one occasion was a flexor tendon involved. Tenosynovitis was once a serious cause of loss of time. Workers who developed it tended to ignore the condition until it became severe, and at that stage complete immobilization with consequent absence from work was the rule. Unfortunately having left employment and gone outside our control or advice, they remained out, and frequently prolonged complete immobilization resulted in adhesions which further lengthened the period of disability. Further, many patients who had apparently fully recovered, returned to

work, but within a week were again stricken. For some years now our policy has been to encourage workers to report immediately they feel pain about the wrist joint. The diagnosis is usually easily confirmed by feeling crepitus. The forearm, wrist and fingers we partially immobilize with the wrist hyper-extended and the fingers slightly flexed. This is done by means of an adhesive elastic bandage tightly stretched from the elbow to the finger tips. This strip is fixed by another around the upper forearm and one or two bands over the points at which crepitus is felt. Short wave therapy is given for 10 minutes twice each day, and arrangements are made for the worker to draw her average wage so long as she remains at work. In about a week, passive movements and light massage are begun, followed later by active movements; the patient is thus encouraged to accept partial but not complete immobilization, for she returns to her job and works slowly. Of the 63 patients already mentioned only one had not completely recovered within 10 days. She recovered in three weeks on being suspended from work, only coming in, with her arm on a sling, for physiotherapy. Usually pain disappears in three or four days, but the treatment is continued for several more and we now have none of the tedious long term cases which were so common some years ago. Our experience seems therefore to coincide with that of Thompson, Plewes, and Shaw (1951).

Summary

The main processes where hazards occur in the manufacture of cordage, are described. These hazards include a condition which resembles byssinosis, the various skin lesions associated with the use of tar and tar-oils, nerve deafness amongst plaiters similar to boiler maker's deafness, tenosynovitis or peritendenitis crepitans amongst braiders, and various types of accidents.

It is indicated that the industry, because of its history, has been in the past very conservative, but that active steps are now being taken in an attempt to control the various hazards.

I am grateful to my colleagues in the Belfast Ropeworks Ltd., and in particular Mr. A. P. Armstrong and his associates Mr. H. Hodge, Mr. G. Brown, and Mr. W. S. McMeekin not only for information about the processes but also for the historical data about the trade. The knowledge and experience of Sister I. Balmer and of her staff in the Medical Department have been invaluable.

Figs. 1 and 3 were taken by Mr. G. H. Edgar of Messrs. Short Bros. and Harland Ltd., and I am indebted greatly to him for his skill and cooperation. Figure 2 is by the *Belfast Telegraph*, and I am obliged to the Editor for permission to reproduce it.

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AN APPLIANCE FOR THE PREVENTION OF MERCURY POISONING

BY

FRANZ STOCKER

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Occupational mercury poisoning on a large scale is unlikely to be seen by many industrial medical officers in future. This was not always so, for in the latter part of the nineteenth century the condition was common in the metallurgical industries in which mercury was extracted from cinnabar, in mirror manufacture, in fire-gilding, in haircutting, in hat-making, and in the manufacture of thermometers, barometers, and glow-lamps. In these and also in the chemical industry quicksilver poisoning was often severe.

By the introduction of preventive measures, and as a result of the changes in manufacturing methods which were developed about that time, the number of cases was considerably reduced in the subsequent decades. In many undertakings mercury poisoning ceased to exist.

A classical example of such improvement is found in the mirror industry where harmless mercury compounds replaced the pure metal. Weyl (1908) has described this advance and states that in Fürth, then the centre of the German mirror industry, mercurialism had ceased to appear as early as 1907, though, about a decade earlier, it had occurred frequently causing thousands of working hours to be lost.

Technical advances brought fundamental changes in the commercial and industrial structure of all countries, and at the same time a greater degree of safety in previously dangerous occupations. Nevertheless new possibilities of injury to health were arising.

As examples we may mention the introduction of mechanical drills in mining and tunnelling, the development of modern solvents in various industries and the use of *x*-rays for therapeutic and other purposes. All these have led to diseases which were partly or completely unknown to earlier generations. Doctors employed in industry must therefore be aware of the occupational risks arising from the methods used at any particular period, and must devise means of protecting those workers whose health might be affected, by planning necessary safeguards in the early stages of any new industrial process.

To the rapidly expanding electrical and machine industry, mercury is essential because of its peculiar physical properties. More attention should be paid to the risk of mercury poisoning in the filling, emptying, and repairing of apparatus such as vacuum pumps using mercury, mercury rectifiers or contact breakers, and also mercury vapour lamps and electro-medical apparatus.

Measures usually employed to prevent mercury poisoning include the provision of adequate ventilation and of smooth tables and floors without rifts or crannies, the prohibition of smoking or eating during working hours, an insistence on the washing of hands before meals, as well as a complete and thorough wash when work ceases, the care of the mouth, a medical supervision of various shifts of workers etc.

But it is not always possible to be sure that small quantities of mercury do not escape onto the tables and floor or collect in small rifts or crevices. This may easily occur when apparatus used in physics or in the electrical industry, such as thermometers and barometers, are being manipulated. If the ventilation is inadequate, which is often the case in small factories, particularly in winter, it means that the workmen are obliged to spend many months in an atmosphere containing mercury vapour.

This paper describes an appliance for collecting spilled mercury, used for many years by Siemens and Halske of Vienna, manufacturers of wireless transmitters, electrical machines, measuring equipment, and similar apparatus. In its testing departments specially trained technicians examine the articles manufactured before delivery. Fig. 1

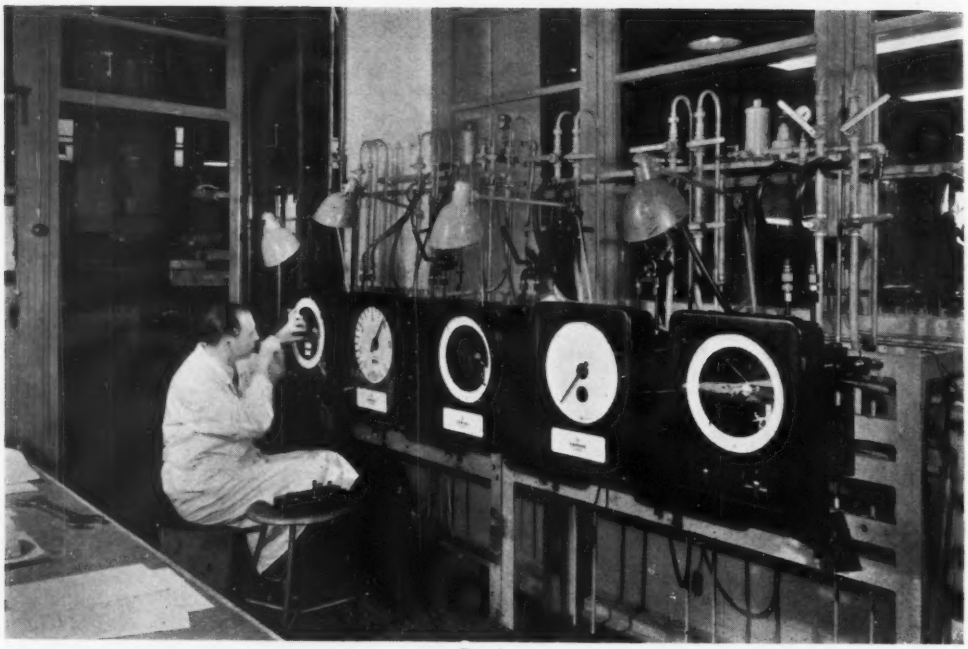

FIG. 1

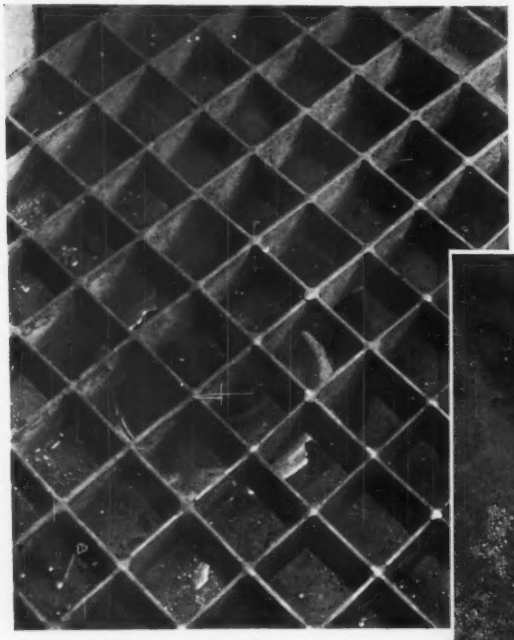

FIG. 2

FIG. 1.—Test room for calibrating pressure gauges and other apparatus.

FIG. 2.—Basin for collecting loose mercury.

FIG. 3.—Overflow and emptying plug for the basin; the gutter for collecting mercury is also shown.

FIG. 3

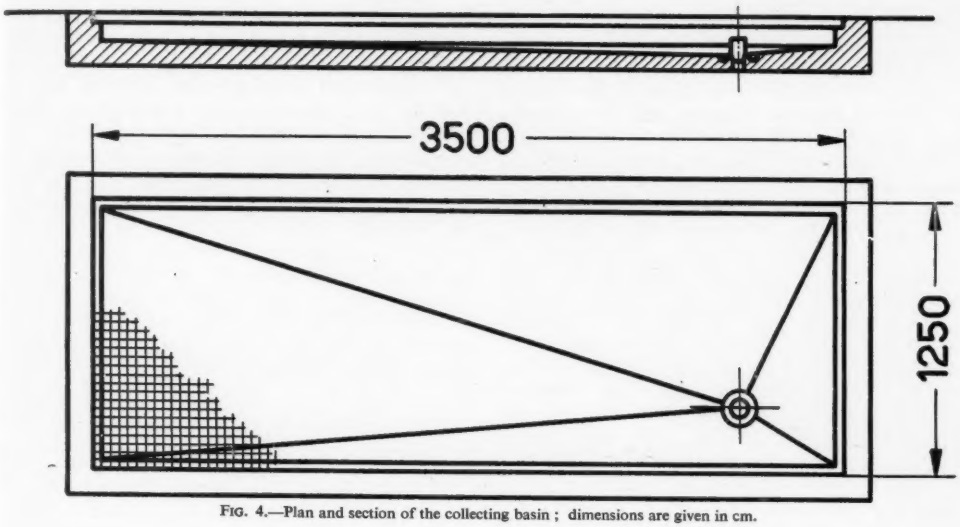

FIG. 4.—Plan and section of the collecting basin ; dimensions are given in cm.

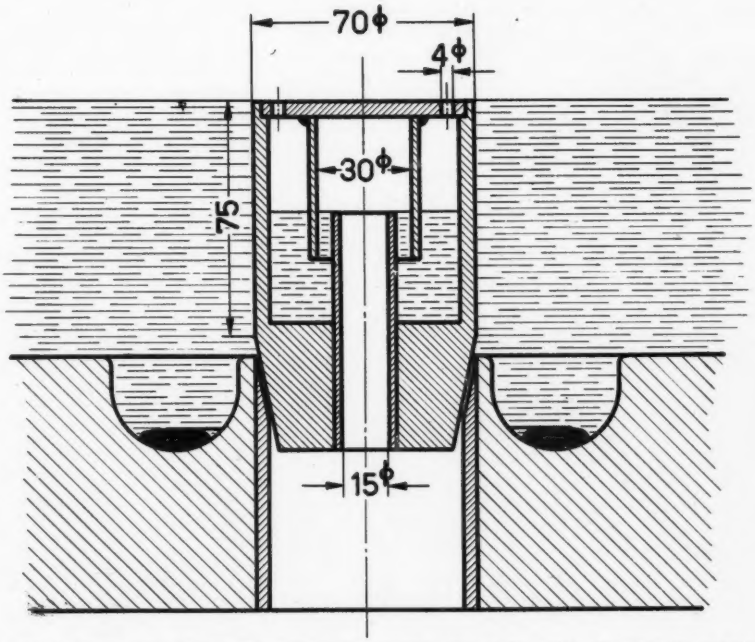

FIG. 5.—Cross-section through the overflow and emptying plug of the basin ; the gutter for collecting mercury is also illustrated.

shows one of these departments in which experts calibrate pressure gauges and apparatus used for quantity measurements. The apparatus contains up to 5 kg. of mercury which is put into it and withdrawn by the operative. Even if the greatest possible care is taken, it is very difficult to prevent some drops of mercury from falling on the floor. A very simple safety device has made it possible to control this hazard. It consists of a large basin full of water which is let into the floor beneath the working point (Fig. 1) covered by an iron grill (Fig. 2). If, as often happens, some mercury is scattered while an apparatus under test is being filled or emptied, then the metal will fall through the grill into the basin which contains water. Fig. 3 shows the quantity of mercury which has fallen into the basin during a fairly short working period. The water is "syphoned off" through the plug in the centre of the gutter in which the mercury collects. The mercury is then easily removed and purified for further use.

Fuller details of the design and dimensions of the collecting trough are given in Figs. 4 and 5.

This apparatus has proved to be successful. The employee is completely protected, and is spared the anxiety and dangers of an insidious hazard. Because of its low cost the installation can easily be used by small firms, and it also represents an economy as mercury is recovered. The costs of medical examination by the authorities charged with industrial welfare are also saved. Such costs are normally borne by the employer, but are avoidable and can be considerably reduced when the precautions described are taken. The method described has already proved to be of value in preventing mercury poisoning, and for this reason we feel justified in making this appliance more widely known in industrial circles.

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CONTRIBUTION A L'ETUDE DE LA TOXICOLOGIE DU TRICHLORETHYLENE

I. DOSAGE DANS LES MILIEUX BIOLOGIQUES

PAR

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L'étude de la toxicologie du trichloréthylène, $CHCl–CCl_2$, constitue, du fait de l'extension toujours croissante des emplois de ce solvant (extraction des graisses, dissolution des peintures et vernis, dégraissage des pièces métalliques, nettoyage à sec des étoffes, etc.) un problème d'hygiène industrielle de grande actualité. Par suite de l'utilisation depuis quelques années, de ce dérivé chloré de l'acétylène comme anesthésique, une telle étude est devenue également fort importante dans le domaine thérapeutique. On avait cru tout d'abord qu'il s'agissait d'un produit dépourvu de toxicité. C'était là l'opinion d'Ullmann (1928) et aussi de Trillat (1937) dans son rapport au conseil supérieur d'hygiène publique de France. Dès 1915, toutefois, Plessner (1916) avait décrit plusieurs cas d'intoxication chronique et Brezina et Teleky (1921a, b, 1922) indiquaient que son action prolongée exerçait un effet nocif sur l'organisme.

De fait, de 1914 à 1931, 284 cas d'intoxication, dont 25 mortels, furent relevés en Allemagne par Stüber (1931) (202 intoxications aiguës, et 82 intoxications chroniques). En Angleterre, l'Inspection du Travail releva de 1923 à 1935 39 cas d'intoxication, dont trois mortels.

En France, Carrieu (1927) signala, en 1926, cinq cas mortels auxquels Vallée et Leclercq (1935) ajoutèrent un sixième en 1935.

Depuis cette époque, le trichloréthylène a continué, dans tous les pays, à provoquer des accidents. Il n'est pas étonnant, dans ces conditions, que les toxicologues et les hygiénistes lui aient consacré de nombreuses recherches. Elles ont conduit à préciser entre autres les transformations subies dans l'organisme par ce solvant chloré. Barrett en collaboration avec Cunningham et Johnston (1939) réussit à montrer que, chez le chien, une partie au moins du trichloréthylène était transformée, suivant un mécanisme d'ailleurs non élucidé, en acide trichloracétique :

$$\underset{\text{trichloréthylène}}{CHCl = CCl_2} \rightarrow \underset{\text{acide trichloracétique}}{CCl_3\,CO_2H}$$

qu'il isola sous forme de di (trichloracétate) de pipérazine. Powell (1945) démontra qu'il en était de même chez l'homme.*

Dans l'intoxication par le trichloréthylène, il faut donc, comme dans le cas de beaucoup d'autres substances toxiques (Fabre et Truhaut, 1949) rechercher et doser, non seulement le toxique intact, mais encore le produit de son métabolisme.

Nos efforts ont tendu tout d'abord a établir une méthode permettant de façon satisfaisante le dosage successif du trichloréthylène et de l'acide trichloracétique dans les produits biologiques. Son exposé constitue l'objet du présent article. Dans une prochaine publication, nous présenterons les résultats que nous avons obtenus en l'appliquant à l'étude de l'intoxication expérimentale aiguë ou chronique par le trichloréthylène.

Dosage du Trichloréthylène et de l'Acide Trichloracétique dans les Produits Biologiques

Dosage du Trichloréthylène : Méthode de R. Truhaut (1951).—La technique comporte trois phases successives.

Entraînement du Toxique par un Courant d'Air Chaud.—Ce principe a été appliqué par l'un de nous (Fabre, 1944) au dosage, dans les milieux biologiques, de solvants comme le benzène ou le sulfure de carbone qui, en raison de leur grande affinité pour les lipides, ne sont qu'incomplètement séparés par la vapeur

Tout récemment, Butler (1949) a indiqué que dans l'urine de chien soumis à l'inhalation de trichloréthylène, on pouvait, par hydrolyse acide à chaud, obtenir du trichloréthanol en proportion plus importante que l'acide trichloracétique. D'après lui les deux métabolites pourraient dériver de l'hydrate de chloral préalablement formé à partir du trichloréthylène et l'on aurait, au moins chez le chien, le schéma suivant de transformation métabolique du solvant :

Trichloréthylène
↓
Hydrate de chloral
↙ ↘
Trichloréthanol Acide trichloracétique

d'eau. La température du courant d'air doit être de 50°, c'est-à-dire inférieure à celle provoquant la coagulation des protéides du sang et des organes. Par ailleurs, pour que la totalité du solvant volatil soit entraînée, même si l'on part de milieux très riches en lipides, il faut diviser finement le courant gazeux. Dans ce but, on utilise l'appareillage spécial antérieurement décrit (Fabre, 1944). L'échantillon de sang ou d'organes exactement pesé est introduit dans un tube A d'environ 20 mm. de diamètre, limité à sa partie inférieure par une plaque de verre fritté B, sertie dans le tube. A la partie inférieure de ce tube est soudé un tube de très faible diamètre (2 à 3 mm.) C permettant l'accès de l'air qui devra traverser la plaque de verre fritté en fines bulles gazeuses réparties sur toute la surface (Fig. 1).

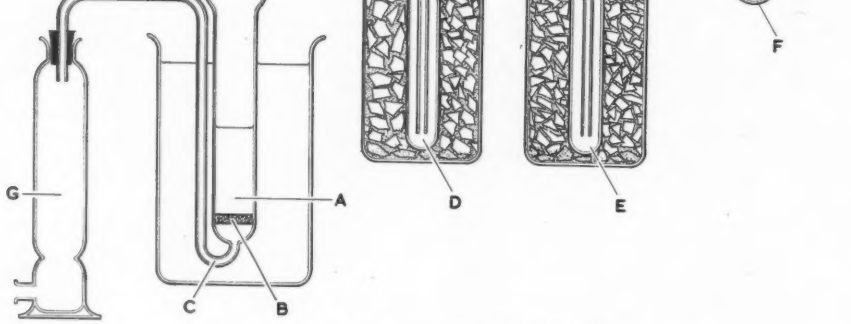

Fig. 1.—Appareil pour le dosage du trichloréthylène dans le sang et les organes.

L'ensemble des tubes A et C est plongé dans un thermostat maintenu à 50°. La partie supérieure du tube A est reliée par rodage à deux barboteurs D et E montés en série ; 10 cm.3 de pyridine sont introduits dans le premier et 5 cm.3 dans le second et chacun d'eux est plongé dans un cristallisoir contenant un mélange glace + sel. A la suite sont placés un barboteur de garde du type Maquenne F et un régulateur de *Jungfleisch*, lequel est relié à une trompe à eau dont on règle le débit grâce à une pince de Mohr de façon qu'il passe une ou deux bulles seulement par seconde, soit environ 10 litres par heure. L'entrainement est poursuivi pendant 2 heures 30. La prise d'essai de matériel biologique peut varier de 1 à 10 g. Quand il s'agit d'organes, il faut procéder au préalable à leur pulpation en opérant à basse température, de façon à éviter toute perte par volatilisation. La pulpe est ensuite mise en suspension dans du soluté physiologique (5 cm.3 pour 1 g. d'organe). Quand il s'agit d'un dosage dans le sang, il faut recueillir ce dernier sur fluorure de sodium (0,05 environ pour 10 cm.3 de sang). On dilue ensuite au demi avec de l'eau distillée. Pour éviter la formation de mousse lors du passage de l'air, il est bon, dans tous les cas, d'ajouter une goutte d'alcool octylique ou un peu de suspension à 10 p. 100 de stéarate de calcium dans l'huile de vaseline (1 cm.3 pour 10 cm.3 de sang dilué au demi ou de suspension d'organes).

Pour éviter l'interférence de vapeurs de solvants chlorés pouvant exister dans l'atmosphère du laboratoire où est pratiqué le dosage, il est recommandé de faire prédéder le tube A d'une colonne G garnie de charbon actif.

Captation du Trichloréthylène.—Les procédés proposés antérieurement faisaient appel, soit à l'adsorption sur charbons actifs ou sur silicagel, Fabre et Mlle. de Belvata Balasy (1949), avec élution ultérieure à l'aide d'un solvant convenablement choisi, soit à la dissolution directe dans certains solvants, par exemple : l'alcool éthylique (Barrett, 1936), le toluène (Habgood et Powell, 1945), ou l'anisol (Brain et Helliwell, 1949), étant donné le mécanisme de la réaction colorée utilisée, dont le premier stade est la formation d'un pyridinium par addition du composé halogéné sur l'azote de la pyridine (Truhaut, 1949), il nous a semblé logique d'essayer de retenir le solvant chloré par barbotage dans la pyridine remplaçant ainsi les deux phases d'adsorption et d'élution par une seule phase de captation. Pour que cette captation soit totale, il faut monter deux barboteurs en série et surtout les refroidir, non pas seulement dans la glace fondante mais dans un mélange glace + sel.

La pyridine utilisée doit être soumise à un essai à blanc ; certains échantillons de pyridine donnent en

effet directement une coloration par chauffage avec une solution alcaline. Il faut, dans ce cas, purifier la pyridine en la portant à l'ébullition au réfrigérant à reflux pendant une demi-heure avec 1/20éme environ de son poids de potasse en pastilles et recueillant ensuite les fractions qui passent à la distillation à 114–115°.

Dosage Photométrique.—Il est basé sur la coloration rouge violacée que donne le trichloréthylène par chauffage avec la pyridine en milieu alcalin (Bruning et Schnetka, 1934). Il faut se souvenir que des colorations analogues ou voisines sont fournies dans les mêmes conditions par divers composés halogénés et, en particulier, dans la série des solvants chlorés, par le chloroforme, le tétrachlorure de carbone, et le tétrachloréthane. Dans un travail antérieurement publié, l'un de nous (Truhaut, 1949), à la lumière de résultats personnels et de travaux antérieurs, a précisé le mécanisme et les limites de spécificité de cette réaction colorée alcalino-pyridinique signalée pour la première fois par Fujiwara (1914) dans le cas du chloroforme et considérée à tort, à la suite de Ross (1923), comme spécifique d'un groupement trihalogéné R–C $\equiv X_3$.

Elle a été appliquée par divers auteurs au dosage du solvant chloré, soit dans les atmosphères (Barrett, 1936 ; Brain, 1949), soit dans les milieux biologiques (Bruning et Schnetka, 1934 ; Barrett, Cunningham, et Johnston, 1939 ; Barrett et Johnston, 1939 ; Habgood et Powell, 1945 ; Forssman et Ahlmark, 1946 ; Fabre et de Balasy, 1949 ; Brain et Helliwell, 1949 ; Frant et Westendorp, 1950).

Toutes ces techniques sont basées sur le développement de la coloration en phase hétérogène. Aucune ne nous a donné entière satisfaction, surtout à cause de l'instabilité de la matière colorante formée et de la production, dans la couche pyridinique, d'une opalescence gênant l'évaluation photométrique. Cet inconvénient disparaît en pratiquant la réaction suivant le mode opératoire original, en phase homogène hydro-alcoolique, préconisé par Truhaut (1949), qui présente le double avantage d'atteindre une sensibilité beaucoup plus grande (ordre du γ par cm.3 de pyridine) et d'augmenter la spécificité (le chloroforme et le tétrachlorure de carbone ne gênent que pour des doses relativement élevées).

Voici les détails de la technique : on mélange avec soin le contenu des deux barboteurs. On prélève ensuite 5 cm.3 de solution pyridinique que l'on additionne de 1 cm.3 de solution de soude à 1 p. 100 dans l'alcool à 95°. On porte au bain-marie bouillant à 70° pendant trois minutes exactement, on refroidit sous un courant d'eau froide, on ajoute 3 cm.3 d'eau distillée et on mélange. Au bout d'une minute à une minute trente secondes et *sans attendre plus de trois minutes*, on doit effectuer la lecture photométrique car, à partir de la troisième minute, la coloration commence à décroître lentement. On se reporte ensuite à une courbe d'étalonnage obtenue à l'aide d'une solution pyridinique de trichloréthylène de concentration connue. Voici celle que nous avons établie en utilisant le photomètre de Pulfrich avec écran vert S 53 et cuve de 10 mm, la cuve témoin étant remplie avec un mélange de pyridine (5 vol.) + solution alcoolique de soude à 1 p. 100 (1 vol.) + eau (3 vol.). On voit que, entre 0 et 200 γ de trichloréthylène dans 5 cm.3 de pyridine, la courbe est une droite (Fig. 2).

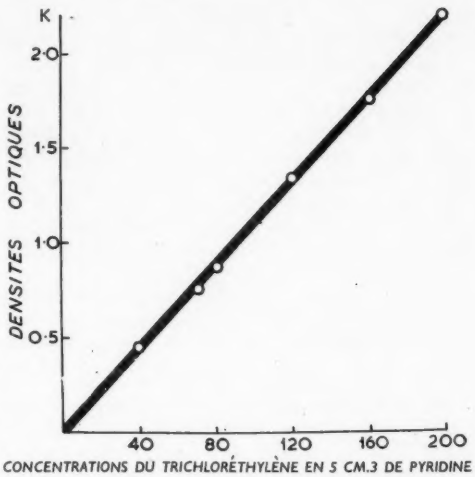

Fig. 2.—Courbe d'étalonnage établie pour le dosage du trichloréthylène (Photomètre de Pulfrich. Ecran vert S 53. Cuve de 10 mm.).

Dosage de l'Acide Trichloracétique.—Cette méthode a été préconisée par Powell (1945), pour le sang et appliquée aux organes par Fabre et de Balasy (1949). La technique comporte deux phases : défécation du résidu provenant de l'entraînement à l'air chaud ; et dosage photométrique sur le filtrat de défécation basée, comme celui du trichloréthylène, sur la réaction développée par chauffage avec la pyridine en milieu alcalin. La coloration diffère un peu qualitativement de celle fournie par le trichloréthylène et surtout elle se développe moins rapidement. Aussi, faut-il opérer à la température du bain-marie bouillant et augmenter le temps de chauffe.

Pour effectuer la défécation verser sur un filtre le résidu contenu dans le tube à entraînement. Prélever une portion aliquote du filtrat, soit 5 cm.3. Déféquer, dans le cas de pulpe d'organes, par addition de 0 cm.3 5 de tungstate de sodium a 10 p. 100 et 0 cm.3 5 de SO_4H_2N.

S'il s'agit de sang, la défécation demande une quantité plus grande de réactif et, pour le même volume, il faut ajouter 2 cm.3 de tungstate de sodium à 10 p. 100 et 2 cm.3 de SO_4H_2N. Filtrer.

Pour le dosage colorimétrique prélever 1 cm.3 de filtrat et ajouter successivement 10 cm.3 de pyridine ; 1 cm.3 de toluène ; et, après mélange, 5 cm.3 de soude à 35 p. 100. Agiter et porter au bain-marie bouillant 15 minutes en agitant fréquemment.

Apprécier l'intensité de la coloration au photomètre. Se référer à une courbe d'étalonnage établie au préalable à l'aide d'une solution aquense titrée d'acide trichloracétique et, en tenant compte des dilutions successives, en déduire la quantité d'acide trichloracétique contenue dans le poids du prélèvement.

Conclusions

Nous avons établi une méthode pour le dosage simultané dans les milieux biologiques du trichloréthylène et de l'acide trichloracétique. Après avoir entraîné le trichloréthylène par un courant d'air chaud et l'avoir capté dans la pyridine fortement refroidie, on effectue un dosage photométrique basé sur la réaction colorée alcalinopyridinique de Fujiwara, sensibilisée et rendue plus spécifique grâce à un mode opératoire original en phase hydro-alcoolique homogène. L'acide trichloracétique demeure dans le résidu d'entraînement du trichloréthylène et est dosé séparément après défécation tungstique par une technique photométrique dérivée de celle proposée par Powell dans le cas du sang.

English Summary

We have established a method for the simultaneous estimation of trichlorethylene and trichloracetic acid in biological media. After having driven off the trichlorethylene by a current of warm air and having taken it up in pyridine which has been kept very cold, photometric estimation is carried out by the colour method of Fujiwara employing alkaline pyridine, sensitized and rendered more specific by an original method using a homogeneous water-alcohol phase. Trichloracetic acid remains in the residue after getting rid of the trichlorethylene and is estimated separately by a photometric technique, after precipitation by tungstic acid, derived from that proposed by Powell and used for estimating trichloracetic acid in blood.

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THE TOXICITY OF METHYLAL

BY

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Methylal, $CH_2{<}^{OCH_3}_{OCH_3}$, known also as formal, dimethoxymethane, formaldehyde dimethyl acetal and methylene dimethyl ether, the simplest of the group of acetals, can be prepared very simply by the interaction of formaldehyde and methanol catalyzed by dry hydrogen chloride or even by calcium chloride. It is a clear, thin, mobile liquid, lighter than water, and soluble in water to the extent of one part in three of water. Methylal boils at 42·3° C., melts at — 105° C., has a density of $d\frac{20}{4}$ of 0·8508 and a refractive index of $N\frac{18}{D}$ 1·3589. Until recently, methylal was a substance of little commercial importance. However, it is now available on a tonnage basis, and its characteristics, particularly its excellent solvent properties, have proved of industrial interest. It has also been found useful in the plastics and perfume industries, as well as serving as a special fuel.

Methylal, in common with many other volatile organic substances, has at various times been suggested as an inhalation anaesthetic (Krafft-Ebing, 1888; Dujardin-Beaumetz, 1889; Langgaard, 1888), and as early as 1888 attempts were made to use it for this purpose. However, interest waned for many years, and it was not until much later that Bacq and Dallemagne (1943) made a serious investigation of the anaesthetic action of methylal. Using dogs as experimental animals, these investigators made a comparative study of the influence of both methylal and ether on the respiratory and circulatory systems of dogs, and found methylal as an anaesthetic to be less toxic than ether. Subsequent use of methylal as an anaesthetic in some 22 surgical operations by Bach and Dallemagne (1943) indicated that methylal could be safely used for this purpose, and that the after effects were less than with either chloroform or ether. However, it produced anaesthesia more slowly than ether, and its effect was more transitory.

Apart from these few investigations with regard to its anaesthetic action, no investigation of the toxicity of methylal has been reported.

Experimental Procedure

Guinea-pigs and white Swiss mice from the stock bred at the National Institutes of Health were used as experimental animals. Mature guinea-pigs were used as test animals. The weights of the mice used varied between 15 and 20 g. Approximately equal numbers of males and females were employed in the following experiments.

Apparatus.—The equipment used for inhalation experiments consisted of three 34-l. glass chambers into which diluted methylal vapour was conducted (Fig. 1). Air from the laboratory supply line passed through a pressure regulator valve (A, Fig. 2) in order to buffer any changes within the supply line. The air flow through the flowmeter (C) could be controlled readily by adjusting the needle valves (B). The flowmeters were in turn calibrated to give the calculated concentration within the exposure chambers. Air at the adjusted constant rate of flow was bubbled through a flask (D) containing methylal. This flask was immersed in a constant temperature bath maintained at 22·2° C. The methylal-laden air was then mixed with a metered stream of diluting air, and the mixture then passed through a dry gas meter (E) which had previously been calibrated against a wet gas meter.

Method of Analysis.—Air samples were taken from the sampling outlet (G). Diluted (1 : 100) hydrochloric acid was then added to the flask, and this was allowed to stand overnight in order to permit complete absorption of the methylal by the reagent. The solution was then diluted to 100 ml. with water, and 10 ml. of the diluted solution was transferred to a 100 ml. Nessler tube and made up to 100 ml. with water. Schiff's Reagent (5 ml.) was added to the Nessler tube, and the colour was

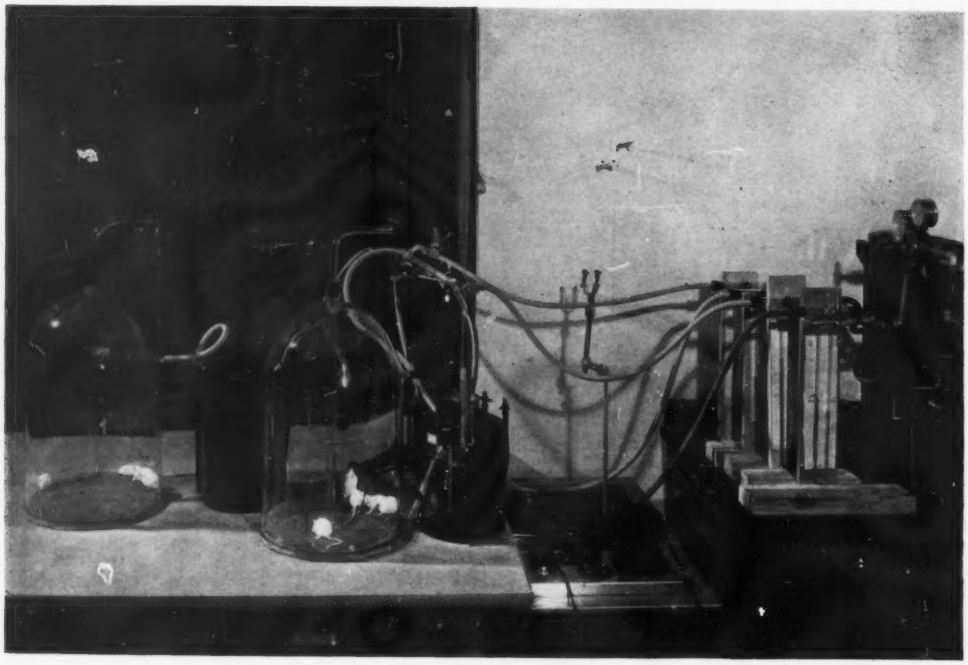

FIG. 1.—Photograph of apparatus.

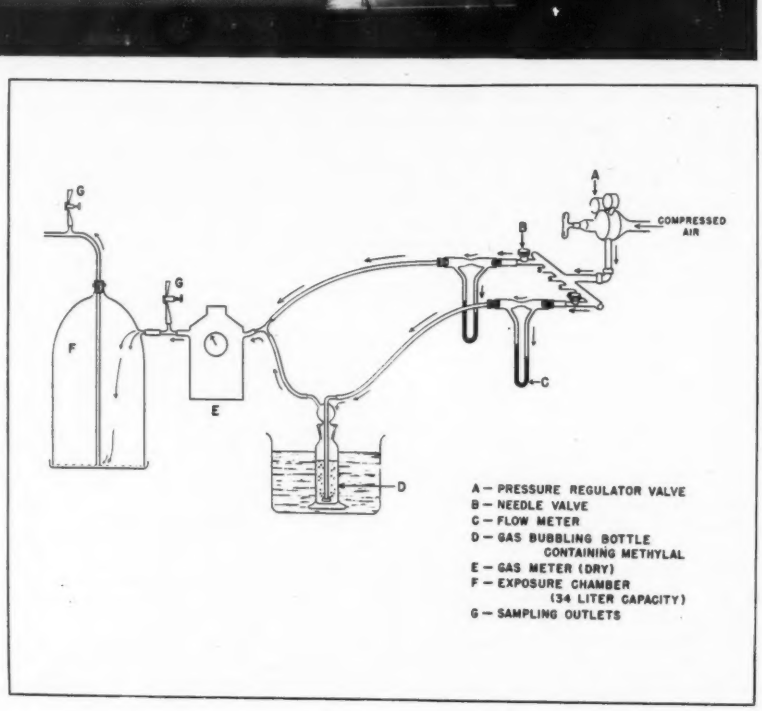

FIG. 2.—Diagrammatic arrangement of apparatus.

llowed to develop for at least 10 minutes. The colour vas then compared with standards prepared under dentical conditions.

Subcutaneous Injection.—The subcutaneous injection of methylal in guinea-pigs was painful at the time of injection, but no apparent discomfort occurred after the injection was completed. Only mild sedative effects and slight impairment of the righting reflex occurred in amounts up to 3 ml. per kg. At levels of 3·5 to 5 ml. per kg. methylal produced anaesthesia within five to 10 minutes, and this effect lasted from three to five hours. At higher levels, anaesthesia was even more immediate, and death occurred following a gradual decrease in rate and depth of respiration.

In guinea-pigs receiving the subcutaneous injection of methylal there was no ill effect apart from a local tissue reaction at the site of the injection. Within two weeks, scab formation progressed to local tissue necrosis and extensive ulceration of 1 to 1½ in. in diameter. This then healed with no further complication.

Acute Toxicity.—Guinea-pigs exposed to very high concentrations of methylal exhibited symptoms of eye and respiratory tract irritation as well as gross incoordination. The irritation was evidenced by vomiting, squinting, lacrimation, sneezing, coughing, and nasal discharge. Death occurred within two to three hours. At measured concentrations slightly above 15% (153,594 p.p.m.), anaesthesia occurred in 20 minutes, and death in one and a half to two and a half hours, and was immediately preceded by slow and irregular respiration. Meyer and Gottlieb-Billroth (1921) established the limiting concentration of methylal for complete narcosis with recovery at 2·8% with an exposure interval of 30 minutes, as compared with a value of 0·44% for chloroform. Meyer and Hemmi (1935) consider methylal to be very similar to ether with reference to its narcotic properties.

Median Lethal Concentration.—Mice in groups of 10 were subjected to varying concentrations of methylal in the exposure chambers, and the death rates were noted for 24 hours following exposure. Where fatalities occurred, these were almost without exception during the exposure period. Eighty per cent of the deaths occurred within the last hour of exposure. With only one exception, all animals surviving the seven-hour exposure period continued to live and thrive.

Within the first 15 minutes of exposure and at the approximate LD_{50} concentration, signs of respiratory tract irritation appeared. Within an hour the mice became excited and progressively more ataxic. In the second hour they were unsteady to the point of being incapable of remaining upright, the fur was ruffled, and the eyes were irritated. Within the third hour, anaesthesia was reached and maintained until the end of the seven-hour period. During anaesthesia the only change noted was in the character of respiration which became progressively more convulsive and irregular. Where death did not occur during exposure, the mice almost invariably survived on removal from the chamber. Approximately two hours of breathing fresh air were required to restore the animals to full consciousness and coordinated control of their extremities. The results of this series of experiments are indicated in Fig. 3, in which each point represents a group of 10 mice. It will be noted that the LD_{50} value is approximately at the concentration of 57 mg. of methylal per l., or 18,354 parts per million. This value is somewhat lower than the value of 28,025 parts per million found by Meyer and Gottlieb-Billroth (1921) to produce complete narcosis. However, the LD_{50} exposure data are based upon continuous exposures of seven hours' duration.

Chronic Exposure.—Large groups of mice were exposed for a seven-hour period daily to methylal vapour over an extended period of time in order to determine whether any pathological changes would result from the inhalation of this substance. Food and water were withheld during the exposure. The control mice were subjected to similar crowded conditions endured by the exposed animals. Three groups of mice were exposed in a different manner.

Series A.—A group of 50 mice received 15 seven-hour exposures to a concentration of methylal averaging 35·1 mg./l. At this concentration methylal proved only mildly irritating. A lack of coordination was apparent only after three or four hours of exposure, and only

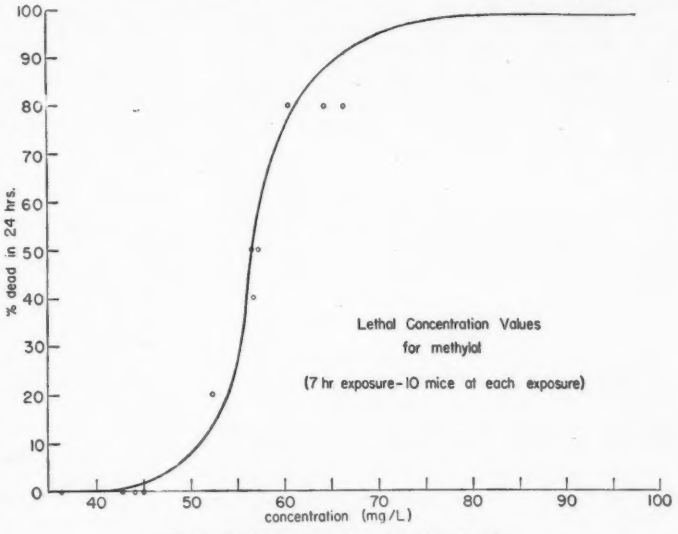

FIG. 3.—Lethal concentration values for methylal.

slight anaesthesia occurred. Recovery was usually complete one hour after removal from the chamber. There were six deaths (all but one of which occurred during exposure) over the 22-day period.

Series B.—A group of 20 mice were given 13 exposures of seven hours each over a 17-day period with methylal averaging 42 mg./l. Irritation was more evident, the anaesthesia time was shorter and anaesthesia deeper, and recovery was slower. The curve (Fig. 4) is somewhat steeper than would be anticipated owing to the difficulty of maintaining a gas concentration at exactly 42 mg./l.

Series C.—A group of 45 mice was subjected to repeated exposures to the LD_{50} value, but the death rate was slightly over 50% for the first two exposures, leaving too few survivors for significant observation.

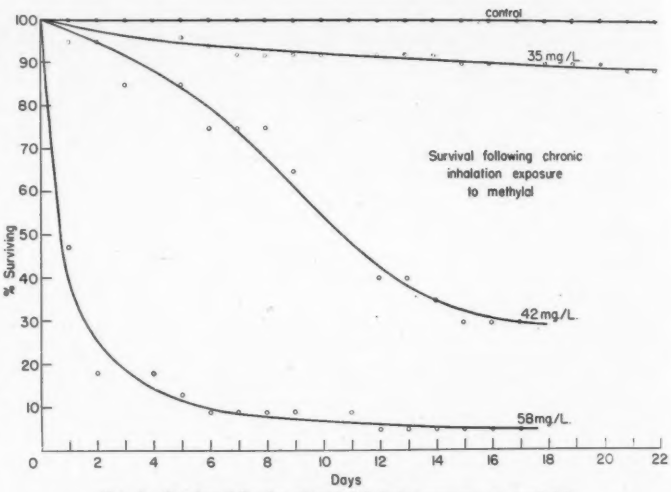

FIG. 4.—Survival following chronic inhalation exposure to methylal.

In Fig. 4 the sharp distinction between the various concentrations is clearly evident. In general the weights of the test animals (particularly at the 35·1 mg./l. concentration) showed no significant variation from those of the controls. Red, white, and differential cell counts and haemoglobin determination on test and control mice revealed no significant variations.

In view of the threshold value of 11,300 p.p.m. of series A and the threshold anaesthesia value of 28,000 p.p.m. reported by Meyer and Gottlieb-Billroth (1921), and by Bacq and Dallemagne (1943), it would appear that one-tenth of this value or 1,000 parts per million would be a safe working concentration.

Metabolism of Methylal.—Experimental investigation did not indicate that the path of methylal excretion was other than that of ordinary respiration. In view of Keeser's (1931) investigation of the metabolism of methanol, tests for formaldehyde and formic acid were made of the vitreous humor and urine. However, there was no indication of the presence of these substances in any case. It is possible, therefore, in view of the stability of methylal in neutral or alkaline media, that methylal is not hydrolyzed at the *p*H of body tissue fluids.

Pathology

The tissues from 14 exposed guinea-pigs, 84 exposed mice, and 30 control mice not exposed to methylal were saved for microscopic study and fixed in formaldehyde. Routine paraffin sections were stained with azure eosinate and Masson's trichrome stain and were examined for haemosiderin after treatment with acidulated potassium ferrocyanide. The eyes were usually enucleated before decalcifying the skulls with formic acid. Frozen sections of the heart, liver, and kidney were stained for fat with oil red (Lillie, 1948).

Five guinea-pigs received a single two to eight-hour inhalation exposure to methylal (over 250 mg./l.). One each died at two and 64 hours, and three were killed at 16, 20, and 74 hours after the beginning of the exposure. The animal that died at two hours showed no significant changes; the other four had moderate to severe fatty degeneration of the liver and kidney, and an extensive bronchopneumonia with polymorphonuclear leucocytes predominating in the alveolar exudate. In addition, two showed moderate fatty degeneration of the myocardium. Three other guinea-pigs killed 23 hours after three successive seven-hour daily inhalation exposures to methylal showed similar changes in the lungs, liver, and kidneys.

Six guinea-pigs were given four to five daily inhalation exposures to methylal (51 to 140 mg./l.), usually seven hours on successive days. They were killed for study about 24 hours after the beginning of the last exposure. Four showed no significant changes, one showed a small area of pneumonia, and one showed a small focus of necrosis in the adrenal cortex.

Six mice were studied at three to 72 hours after beginning a three-hour exposure to 122 mg./l. of methylal, and 25 at six to 154 hours after a six-hour exposure to 88 mg./l. of methylal. Significant changes were found only among 16 mice that were killed at six to 54 hours after beginning the exposure; eight had slight pulmonary congestion, three had pulmonary oedema, and four had slight fatty changes in the liver and kidney.

Fifty-three mice were exposed to methylal seven hours daily except Saturday and Sunday. Four of nine that died after four to 11 exposures to methylal (36 to 87 mg./l.) had a bronchopneumonia and four had slight fatty changes in the liver or kidney. Six mice were killed 40 days after the last of 13 exposures to methylal (34 to 54 mg./l.); four had slight to moderate splenic haemosiderosis, three had pneumonia, and one showed slight fatty changes in the kidney. Twenty of 38 mice were killed 20 hours after the fifteenth exposure to methylal (28 to 45 mg./l.); two each had bronchopneumonia, pulmonary oedema, and pulmonary haemorrhages, and one had slight fatty changes in the kidney. Of the remaining 18 mice, five each were killed at 23 and 30 days, and four each at 44 and 72 days after the last exposure. Eleven of the 18 had slight haemosiderosis of the spleen, and two had slight fatty changes in the kidney.

Pneumonia and other incidental lesions were more common in the exposed mice than in those not exposed, but the incidence of such lesions may vary markedly in different groups of mice. The fatty changes and haemosiderosis are considered non-specific changes; similar changes have been found after exposure to various toxic agents (Highman and Heppel, 1946).

No changes were found in the optic nerve or retina attributable to the methylal. About 10% of both control and exposed mice had rodless retinas, an interesting congenital condition described previously in other strains (Jaffé, 1931). It is characterized by the absence of rods and cones and the outer nuclear and reticular layers of the retina. One exposed animal showed a slight infiltration of the cornea and the anterior chamber mainly by polymorphonuclear leucocytes, and another showed a similar infiltration in the cornea beneath a large sub-epithelial bleb containing some basophilic material. These and other minor corneal changes, seen occasionally in both control and exposed mice, are probably incidental lesions.

Summary

Animals exposed to highly toxic concentrations of methylal often developed severe fatty changes in the liver, kidney, and heart, and inflammatory changes in the lungs. Low concentrations generally produced no significant pathologic changes.

The LD50 value of methylal for male laboratory animals was found to be 57 mg./l. (18,354 parts per million). The threshold appears to be about 11,300 parts per million. It would appear that a reasonable safe working concentration for workers continuously exposed to methylal vapour for an eight-hour working day would be 1,000 parts per million.

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THE EFFECT OF BENZENE AND OF CARBON TETRACHLORIDE ON THE CONCENTRATION OF CERTAIN VITAMINS, FAT, AND NITROGEN IN THE LIVER OF THE RAT*

BY

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This study is concerned with the effects of short term moderate dosages of benzene and of carbon tetrachloride on the content of the liver with respect to vitamins, fat, and nitrogen. The experiments were performed because of our interest in the problem of whether exposures to certain toxic agents of industrial concern alter the nutritional needs of the organism. A change in the ability of an organ or tissue to retain normal amounts of a nutrient is one mechanism by which nutritional needs may be altered. That this mechanism actually exists has been demonstrated with certain carcinogens. Thus Goerner and Goerner (1939) found that the hepatic stores of vitamin A were diminished by dibenzanthracene. A similar effect on riboflavin stores of liver in animals treated with butter yellow (Kensler, Young, and Rhoads, 1942; Miller, 1947), and with acetylaminofluorene has been noted (Griffin, Cook, and Luck, 1949; Wase and Allison, 1950).

Experimental Methods and Procedure

Analytical Methods.—The following methods were used.

Nitrogen.—The micro-Kjeldahl determination was employed with the distillate collected in 2% boric acid and ammonia measured titrimetrically.

Lipid.—Fatty acids and unsaponifiable matter were measured gravimetrically using a procedure essentially that of Leathes and Raper (1925) adapted to a small scale.

Vitamin A.—The procedure was essentially that of Lemley, Brown, Bird, and Emmett (1947).

Thiamine (*Vitamin* B_1).—Bound thiamine was released from liver tissue by treatment with clarase (diastase) in acetate buffer as described by Cheldelin, Eppright, Snell, and Guirard (1942). The vitamin was measured fluorometrically by a modification of the procedure of Hennessy (1941). To help avoid interfering substances which may not be adequately compensated for in the usual non-ferricyanide treated blank, we have employed benzene sulfonyl chloride as suggested by Urban and Goldman (1944). This substance prevents the formation of thiochrome, and its use allows both the blank and the unknown to be treated with alkaline ferricyanide. In treating the blank, the benzene sylfonyl chloride is added before ferricyanide, whereas with the unknown it is added after ferricyanide.

Riboflavin.—Bound riboflavin was released in the manner described for thiamine and the free vitamin was determined by the microbiological method of Snell and Strong (1939).

Niacin.—Homogenized liver was suspended in 1 N sulphuric acid autoclaved at 15 lb. pressure for 15 minutes, cooled, and brought to volume. When ready for assay, an aliquot was neutralized and assayed by the microbiological procedure of Krehl, Strong, and Elvehjem (1943).

Procedure.—Three groups of male rats* were maintained on a pellet stock diet† from weaning until they had reached 60 days of age. They were then placed on a purified diet (Diet 11) of the following composition: casein, 20‡; corn oil, 10; cerelose, 66; salts, 4§; with vitamins incorporated per 100 g. of this

* This study was aided by the Division of Research Grants and Fellowships of the U.S. Public Health Service.

* Rats were randomly distributed from seven litters with as nearly equal distribution as possible of litter-mates among the three groups. Since some of the litters were not matched in each group, the statistical analysis employed treated the mean values of the groups as coming from independent samples.

† Rockland Rat Diet ("D" free).

‡ Borden B3F.

§ USP XIII No. 2.

basal diet as follows: thiamine, 1 mg.; riboflavin, 1 mg.; pyridoxine, 1 mg.; niacin, 1 mg.; calcium pantothenate, 2·5 mg.; folic acid, 0·2 mg.; biotin, 0·002 mg.; choline, 50 mg.; percomorph oil, 0·12 ml.

Eight days later the treatments were started. Group I, the control group, received 0·3 ml. per rat of an 0·9% sodium chloride solution subcutaneously on the same days that group II was injected subcutaneously with 0·3 ml. of benzene per 100 g. of bodyweight, and group III received subcutaneously 0·1 ml. carbon tetrachloride per 100 g. bodyweight. Injections were given on seven of the following nine days. On the tenth day all rats were killed by exsanguination and their livers weighed. Small samples of liver were taken for histological examination and the remainder immediately wrapped and frozen in solid CO_2 until analyzed.

At the conclusion of the experiment Group I consisted of nine rats, Group II of 11 rats, and Group III of 11 rats. Group I rats were restricted in their food intake to maintain weight at approximately the levels of the benzene and CCl_4 treated rats.

Results

In Table 1 are listed the average bodyweights of the three groups during the experiment together with average liver weights expressed on the basis of total bodyweight and per 100 g. of bodyweight. The control animals lost weight slightly as a result of food restriction. The benzene group decreased in weight to a greater extent, while the CCl_4 group maintained weight. The CCl_4 treated group had the heaviest livers, but the benzene-treated rats also had livers which were heavier than those of the controls. Calculation of liver weights per 100 g. of bodyweight did not change this order. Statistical analysis of the liver weights by the "t" test indicated that the differences among groups were highly significant on the basis of both the total and per 100 g. bodyweight (Table 1).

TABLE 1

AVERAGE BODY AND LIVER WEIGHTS* OF THE EXPERIMENTAL GROUPS

Group	Control	Benzene	CCl_4
Number of rats	9	11	11
At 1st day	176	199	187
,, 6th ,,	168	190	192
,, 10th ,,	170	172	192
Total liver weight	5·72 ± 0·23	7·16 ± 0·23	9·68 ± 0·29
Liver weight per 100 g. bodyweight	3·36±0·060	4·17±0·096	5·08±0·180
Difference (g.)		0·81	1·72	0·91
Significance (P)		<0·001	<0·001	<0·001

* Liver and body weights expressed in grams ± = standard error of the mean.

In Table 2 are summarized the results of the analyses for thiamine, riboflavin, niacin, vitamin A, nitrogen, and lipid, all expressed per gram of liver. It is clear that the benzene treatment had no significant effect on the concentration of the vitamins and of the fat; the nitrogen concentration of this group was decreased slightly but significantly below that of the controls. Carbon tetrachloride treatment, on the other hand, caused a significant drop in the concentration of all vitamins and of nitrogen. As was expected, the lipid content increased markedly, and this increase in fatty material undoubtedly accounts for some of the

TABLE 2

EFFECT OF BENZENE AND CARBON TETRACHLORIDE ON LIVER CONCENTRATION OF VITAMINS, NITROGEN, AND LIPID*

Group	No. of Rats	Thiamine (γ)	Riboflavin (γ)	Niacin (γ)	Vitamin A (I.U.)	Nitrogen (mg.)	Lipid (mg.)
I. Control	9	14·6 ± 0·85	38·3 ± 1·84	195·9 ± 11·6	838·4 ± 47·1	27·9 ± 0·55	45·6 ± 1·1
II. Benzene	11	12·8 ± 0·94	33·8 ± 2·79	180·7 ± 5·7	836·1 ± 35·3	25·3 ± 0·79	45·0 ± 1·6
III. CCl_4	11	9·4 ± 0·52	23·3 ± 2·53	134·5 ± 4·9	676·5 ± 36·1	20·1 ± 0·64	166·9 ± 5·9
Mean Differences between Groups and their Significance							
Between control and benzene	diff.	1·8	4·5	15·2	2·3	2·6	0·6
	P	0·18	0·18	0·23	0·55	0·02	0·55
Between control and CCl_4	diff.	5·2	15·0	61·4	161·9	7·8	121·3
	P	<0·001	<0·001	<0·001	0·01	<0·001	<0·001
Between benzene and CCl_4	diff.	3·4	10·5	46·2	159·6	5·2	121·9
	P	<0·001	0·01	<0·001	0·004	<0·001	0·001

* Mean per g. of liver ± Standard error of the mean.

differences in vitamin and nitrogen concentrations.

Calculations made on the basis of estimated fat-free liver weight brings the nutrient concentrations of the CCl_4-treated rats closer to those of the controls (Table 3). However, with the exception of vitamin A, the differences are still considerable. Further calculation on the basis of equal nitrogen content per gram of liver brings the concentrations of the water-soluble vitamins of the two groups much more closely into line with each other (Table 3).

TABLE 3

LIVER CONCENTRATION OF VITAMINS AND NITROGEN OF CCl_4 TREATED RATS* (PERCENTAGE OF CONTROL)

Basis	Thiamine (%)	Riboflavin (%)	Niacin (%)	Vitamin A (%)	Nitrogen (%)
Wet weight*	64·4	61·0	68·8	80·7	72·1
Fat-free†	74·9	71·0	80·3	95·3	83·9
Equal N‡	90·0	84·9	95·0	112·7	100·0

* As actually determined from Table 2.

† Fat free concentrations calculated by multiplying concentrations on wet weight basis by factor of 100 ÷ (100 – mg. neutral fat). Neutral fat value taken as 110% of lipid value as given in Table 2.

‡ The observed values of CCl_4 treated livers (Table 2) were multiplied by 1·39 ; i.e. N content of controls ÷ N content of CCl_4 treated rats.

Despite the differences observed in concentration of nutrients per gram of liver, calculation of the total liver content revealed that the CCl_4 group had as much or more of each of the nutrients compared to the benzene and control groups (Table 4). The content of the water-soluble vitamins was not significantly different in the three groups, but there was a significantly greater amount of fat, vitamin A, and nitrogen in the larger liver of the CCl_4-treated rats. The same tendency was noted for the latter three substances in the livers of the benzene-treated animals ; fat and vitamin A content were significantly higher than in the controls while the nitrogen increase was of doubtful significance ($P = \cdot07$).

Histological examination of the livers of a number of the rats was made following fixation in Bouin's solution and staining with hematoxylin-eosin. In all seven of the 11 rats treated with CCl_4, whose livers were examined, there was marked fatty infiltration ; six showed varying degrees of necrosis of the central half of the liver lobule while the seventh animal had all of the lobule involved except a narrow zone in the portal area. Of the six benzene-treated animals examined, the liver showed no obvious changes in four, while in two there was a slight fatty infiltration of cells about the central veins. Livers of the nine control rats appeared normal.

Discussion

The interesting point in this study is that despite rather marked reductions in the vitamin concentrations per gram of liver of CCl_4-treated rats, the overall contents in the liver were as great as, or greater, than in the controls. One question that arises is whether the vitamins in the damaged livers are as available to the organism as those of normal animals. Some attention has been given to this problem by other investigators in the case of vitamin A. Popper, Steigmann, and Dyniewicz, (1942) studied the distribution of this vitamin, using fluorescence microscopy, in the livers of CCl_4-treated rats. They noted that the vitamin tended to accumulate rather quickly in areas of fatty degeneration and less rapidly in normal sites. Chemically, less vitamin A was stored in the liver of vitamin A-deficient rats with CCl_4 intoxication than in non-poisoned control deficient rats following vitamin A feeding. They suggest that the CCl_4-damaged liver releases its vitamin A more slowly than does normal hepatic tissue with resulting lowered plasma levels.

Haig and Post (1941) analyzed the livers of rats for vitamin A three months following an eight-week period of CCl_4 administration. They found no correlation between the concentration of vitamin A in the cirrhotic livers, the liver weight, or the degree of fibrosis ; however, the livers of the

TABLE 4

EFFECT OF BENZENE AND CARBON TETRACHLORIDE ON NUTRIENT CONTENT OF TOTAL RAT LIVER*

Group	Mean Liver Weight (g.)	Thiamine (γ)	Riboflavin (γ)	Niacin (γ)	Vitamin A (I.U.)	Nitrogen (mg.)	Lipid (mg.)
I. Control	5·72	83 ± 5·1	219 ± 12	1114 ± 78	4789 ± 317	162 ± 7·4	257 ± 12
II. Benzene	7·16	91 ± 6·1	240 ± 19	1291 ± 51	5957 ± 251	181 ± 6·7	325 ± 10
III. CCl_4	9·68	91 ± 6·0	226 ± 15	1298 ± 55	6523 ± 468	193 ± 6·5	1622 ± 117

* (Mean ± Standard Error.)

treated animals contained much less vitamin A than did those of the controls. These studies suggest the need for serial studies of plasma vitamin A levels, liver vitamin A content, and histological structure in order to correlate vitamin availability and storage with the changing morphology of the damaged and healing liver.

One would expect much higher vitamin A concentrations in the livers of the CCl_4-treated animals than in those of the controls if vitamin A is deposited preferentially in areas of fatty degeneration, as Popper and others (1942) have described. Our results were to the contrary, but we draw no definite conclusions on this aspect, since vitamin A intake was not rigidly controlled in our study. It should be noted also that there did not appear to be any correlation between total liver fat and total vitamin A. The CCl_4-treated rats had an increase in total fat above the controls of over 500% associated with a vitamin A increase of 36%; the benzene-treated rats had an increase in total fat above controls of only 26% associated with an increased vitamin A of 24%.

Summary

The effects of moderate subcutaneous doses of benzene and of carbon tetrachloride administered over a period of nine days have been investigated with respect to changes in the concentration and total content of thiamine, riboflavin, niacin, vitamin A, fat, and total nitrogen in the livers of rats.

Carbon tetrachloride caused a marked increase in liver weight and liver fat. On the other hand, there was a significant decrease in the concentration of the vitamins and nitrogen per gram of liver. Benzene treatment had no significant effect on the concentration of vitamins, but was associated with a slight decrease in nitrogen concentration and some increase in liver weight.

Because of the increased weight of the livers in the CCl_4-treated rats, the total amounts of the water-soluble vitamins in the livers of this group were about the same as in the livers of the benzene and control groups. Total vitamin A was greater in the CCl_4- and benzene-treated groups than in the controls, but the increases were not proportional to change in total liver fat.

Histologically, the changes in nutrient concentration in the livers of the CCl_4-treated rats were associated with marked fatty infiltration and necrosis of the central half of the liver lobule. Of the benzene-treated rats whose livers were studied, there were no obvious changes in the majority, while some showed slight fatty infiltration about the central veins.

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Brit. J. industr. Med., 1951, **8**, 288.

PLASTIC SPLINTS AND APPLIANCES IN INDUSTRIAL ORTHOPAEDICS

BY

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Many patients with orthopaedic conditions are able to continue their normal work if they are supplied with a light weight splint. In many instances they must be capable of withstanding the various cutting, grinding, cooling, and lubricating fluids which cause plaster of Paris to disintegrate rapidly.

It is only proposed to mention ambulatory appliances, although methods of manufacture and materials are equally applicable to " bed splints ".

The materials to be described are not suitable for instruments such as walking calipers, as at present there is no synthetic material equivalent in strength to steel on a volume for volume basis.

The orthopaedic surgeon and industrial medical officer have to treat two main groups of patients : (1) those who suffer an injury requiring prompt application of an immobilizing splint, e.g., a fractured scaphoid, for which a negative plaster cast cannot be taken ; and (2) those who are suffering from a condition which may require (a) partial immobilization, and limitation of movement (e.g., tenosynovitis, sciatica) ; (b) prevention of deformity (e.g., peripheral nerve injuries) ; and (c) assistance in restoration of function (e.g., tendon repair or amputations).

Properties

Materials used for splint manufacture should possess the following properties : ease and speed of manipulation, durability, resistance to fatigue strain, light weight, inertness to chemical agents, porosity and cheapness, freedom from irritants causing dermatitis, and, in some cases, radiolucency.

A number of synthetic materials come nearer to the ideal than the traditional moulded leather and " celluloid " which must be reinforced with duralumin or steel. The ideal plastic will be one which, after direct application to a patient or mould, will polymerize rapidly to form a rigid, or in some cases a semi-rigid cast or, alternatively, one which is soluble in a high concentration, about 80%, in a cheap solvent such as water. The setting time should not exceed 15 to 20 minutes.

Materials and Manipulation

Cellulose Acetate and Glass Fabric*.—This type of bandage was first described by Kulowski, French, and Erickson (1944) and has been widely used in the United States of America. It is produced as a knitted bandage in varying widths, and consists of 20% glass fibre and 80% cellulose acetate. When quickly dipped into a setting fluid which contains acetone, methylsalicylate, and pentane, the acetate becomes partially soluble and the bandage can be readily applied. Stockinette should be used under the bandage so that the ends of the splint may be finished off by turning the stockinette back over the free edge in order to prevent the glass fibre from irritating the skin. The bandage must be applied with minimum tension, each layer being well smoothed into the preceding one. Moulding is improved if a crepe bandage is wrapped round the cast and held in position for a few minutes after applying the final layer. Setting time is reduced by playing a current of warm air over the surface. The maximum strength of the cast is not achieved for 24 hours, as is also the case with plaster of Paris. " Immobilization time " is longer than with plaster. The cast is inflammable until all fluid has evaporated, and the patient should not be allowed to come into contact with any process where there are naked lights. After this, the risk is no greater than with wood. The finished splint (Fig. 1) is light, porous, unaffected by water, and radio-translucent. Non-bivalved tubular splints are very satisfactory if care is taken in their production. Although a slight *x*-ray shadow is caused by the material,

* Cellulose acetate and glass fabric is produced in Great Britain by John T. Smith & Nephew Ltd., Hull, under the trade name of Glassona. Manufactured in the United States of America by the Tower Co. Inc., Seattle, U.S.A., under the trade name of Airlite.

FIG. 1

FIG. 2

FIG. 1.—"Glassona" scaphoid cast.

FIG. 2.—Polythene wrist splint.

fracture repair can be followed without removal of the appliance, although a final check radiograph, especially for a fractured scaphoid, should be carried out after the cast has been removed.

Immersion in water has no effect on the splint; the stockinette, however, takes some time to dry out. This material is very useful for arm and leg encircling splints (Group 1).

Polyethylene (Polythene)*.—Polythene is the chemical name of a thermoplastic material used in industry for electrical insulation, chemical ware, and for other applications where an inert, semi-rigid material is required. In sheet form it is admirable for the manufacture of appliances which do not require to be completely rigid, e.g., cervical collars and forearm splints (Fig. 2). It is a solid polymer of the gas ethylene, melting at 120°C. At normal body temperature it is tough and somewhat flexible. It is one of the lighter synthetic materials, having a specific gravity of 0·93. It is translucent to light in all parts of the spectrum. Splints do not require to be removed during sunlight treatment. It is unaffected at body temperature by all organic solvents, but over some months of wear it may develop a slight yellowish tinge. This is due to ultra-violet light oxidation, but the strength and durability of the material do not appear to be impaired. A flesh-tinted polythene containing an anti-oxident is now available for medical purposes.

Manipulation of Sheet Polythene.—The most suitable thicknesses of sheet are $\frac{1}{8}$ in. and $\frac{3}{16}$ in. A spinal jacket will be used to illustrate the procedure, the jacket being moulded in two halves.

Overall measurements of the positive plaster cast are taken, and two pieces of polythene of the

* Polyethylene (Polythene) is produced in England by Imperial Chemical Industries Ltd. (Plastics Division), under the trade name of Alkathene.

appropriate sizes are cut. Offcuts of the material are used as reinforcements, as most jackets require to be strengthened down the spine. The sheet is placed on a perforated asbestos board which has been lightly dusted with French chalk (Fig. 3). This powder acts as a "release" preventing the softened polythene from adhering to the asbestos. The reinforcing strip is placed in the position required, the areas of contact having previously been cleaned with benzene. It is absolutely essential that no powder or grease is allowed to remain between the opposed surfaces, otherwise satisfactory fusion will not take place. The asbestos board and polythene are placed in an oven, preferably with a thermostat set at 120°C., and left until the sheet and reinforcing strip are completely transparent. The rate of heating should not be too rapid, otherwise bubbling occurs. When ready for moulding, the polythene is in a semi-viscous state. A piece of stockinette of the appropriate size which has been dusted with French chalk is stretched carefully into position. The edges of the reinforcing strip are pressed into the underlying sheet (Fig. 4). The stockinette and polythene are applied to the plaster cast (Fig. 4*a*). A thin sheet of "durestos" (described later) allows slower and more regular cooling of the polythene, and thus prevents the inside of the moulding wrinkling. It is advisable to allow the polythene to remain in position on the cast for about $\frac{3}{4}$ hour. The imprint of the stockinette is left on the outside of the polythene, and this is preferred by patients to the smooth, wax-like feel of the original sheet.

A strip of polythene is moulded to form a hinge and riveted with tubular, bifurcated, nickel-plated rivets. A locking zip-fastener attached to a lacing is fitted to the other side of the jacket. This lacing adjustment allows for any increase in size of the patient, and the zip-fastener is the most simple method for everyday application of the appliance (Figs. 5 and 6).

With the exception of an oven, no expensive equipment is required. Splints are far quicker to produce than similar appliances made from moulded leather or cellulose acetate reinforced with steel. The cost of production is approximately half. They are light in weight and are readily kept clean. At the present time, all old appliances are reclaimable for scrap.

"Durestos" (Resinated Asbestos Felt).–"Durestos" is a thermosetting, laminating felt used in industry for the manufacture of many lightweight components. It consists of asbestos fibre which has been treated with partially condensed phenolformaldehyde resin. This resin, on further heating, condenses to form an insoluble solid, the asbestos acting as a reinforcing filler. The sheets are available in three thicknesses and become workable when they are damped with water. The resin is soluble in spirit or acetone and these may be used as alternative wetting agents. Care must be taken, however, that the moulding is not placed in the oven before inflammable solvents have evaporated.

Preparation of the Cast.—The plaster cast is painted with a solution of cellulose acetate, and then wiped over with a film of petroleum jelly to prevent the resin from penetrating the plaster and to allow of easy removal of the cured moulding.

Manipulation.—A hip spica is used to illustrate the method of manipulating this material.

The required number of pieces are cut from the dry felt and dampened, applying as little water as possible. The felts should be left for approximately a quarter of an hour, after which time it is possible to stretch the material readily in the direction required. If the edges of the material are well teased, satisfactory lap joints can be made (Fig. 7). Great care must be taken, when applying the felts, to ensure that each layer is firmly bonded to the next, and that no air pockets are left between the laminates. Reinforcement is by means of offcuts placed between the laminates in the areas where increased strength is required. A piece of muslin firmly stretched over the last laminate prevents "spring back" of the felts. Strips of muslin are placed in the direction of re-entrant curves to prevent "bowstringing" of the laminates (Fig. 8). A final coat of cellulose acetate solution is applied and the evaporation of the solvent helps in the consolidation of the moulding. Its main purpose, however, is to give a smooth finish to the cured laminate. The cast is placed in an oven, and allowed to cure at 70°C. for about eight to 10 hours. Temperatures above this are liable to cause delamination. The time period depends on the size of the cast and the dryness of the plaster.

The cured splint is cut from the cast with an electric, circular handsaw; $\frac{1}{8}$ in. ventilation holes are drilled, and the inside coated with a water emulsion of unplasticized polyvinyl acetate. It is then put back into the oven for five minutes to form a skin.

After fitting to the patient, the splint is coated with a metal-based cellulose primer, followed by a flesh-coloured cellulose lacquer. Buckles, straps and laces, etc. are then attached (Fig. 9).

Splints may be washed with warm, soapy water, and are unaffected by normal body secretions, sea-

* Durestos (resinated asbestos felt) is produced by Turner Bros., Rochdale, under the trade name of Durestos. It is a phenolformaldehyde resinated asbestos laminating felt.

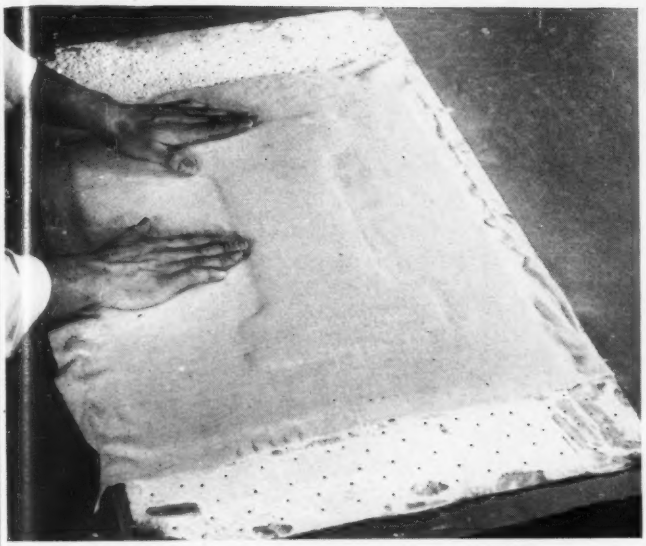

FIG. 3.—Polythene sheet on asbestos board with reinforcing strip in position.

FIG. 3a.—Transparent sheets and reinforcing strip ready for moulding.

FIG. 4.—Application of stockinette to sheet.

FIG. 4a.—Polythene applied to cast.

FIG. 4

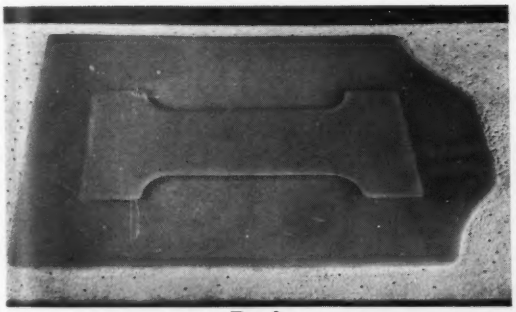

FIG. 3

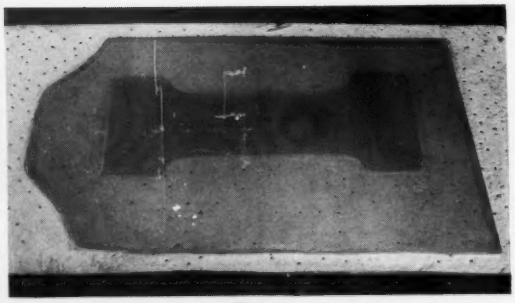

FIG. 3*a*

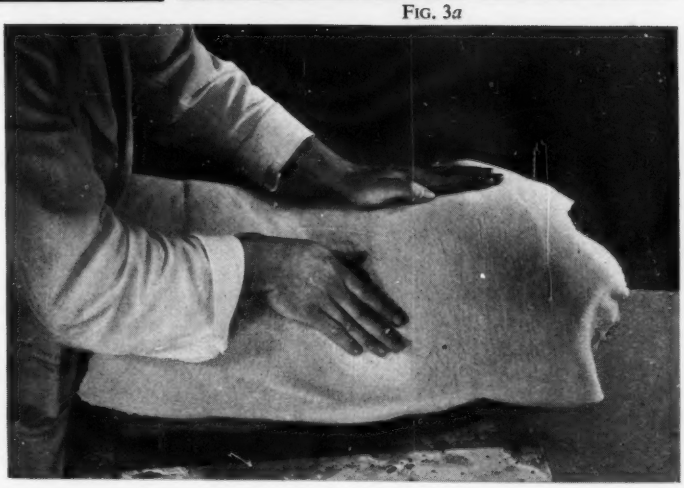

FIG. 4*a*

FIG. 5

FIG. 5.—Finished jacket.

FIG. 6.—Patient after spine graft, wearing polythene jacket with abdominal corset.

FIG. 7.—Application of felt to cast. Note teased edge.

FIG. 8.—Moulding ready for curing. Note position of muslin strips which prevent "bowstringing" of felt across re-entrant curves.

FIG. 6

FIG. 7

FIG. 8

water, etc. They may also be used for treatment in chlorinated swimming pools.

The finished appliance is light in weight, rigid, and requires no metal reinforcement. It does not distort with use and is non-inflammable.

This material is most satisfactory for rigid splints, used in the treatment of patients in Groups 2a and 2c, for example, spicas, pylons, rigid spinal jackets, and long leg gutters (Fig. 10).

There appears to be no risk of contact dermatitis with the cured material and no cases have been reported.

Perspex (Polymethyl Methacrylate)*.—This is a thermoplastic material with a varying degree of rigidity, depending on its thickness. The plasticized sheet material ($\frac{1}{16}$ in. to $\frac{3}{16}$ in.) is most suitable for small splints and parts of rehabilitation appliances (Fig. 11a, b, c), but it is not suitable for large appliances such as pylons or hip spicas, as it is difficult, without suitable equipment, to mould complex shapes and, should the mouldings break, the sharp edges left may cause considerable injuries.

Method of Manipulation.—Small supporting splints can be made either by pressing the material softened by heat between male and female plaster casts, or, if the shape is relatively simple, it can be pressed into contact with a positive plaster cast, the operator wearing asbestos gloves. Minor adjustments can be made by manipulating locally heated areas.

As with polythene, the appropriate size of sheet is prepared and placed on an asbestos board, in any form of oven which will give a temperature of 140°C. The sheet should not be overheated, as breakdown of the material occurs. When ready for moulding it is soft and rubberlike. Unlike polythene, it has considerable " springback " in its mouldable state, and must, therefore, he held in contact with the cast while cooling. Airholes are drilled for ventilation and should be countersunk on the side next to the patient's skin. They should not be more than

* Perspex (Polymethyl methacrylate) is produced in the United Kingdom by Imperial Chemical Industries under the trade name of Perspex. Known in the United States as Lucite and Plexiglas.

FIG. 9.—Finished spica.

FIG. 10.—Dwarf, with fibrous dysplasia of bone, who had had bilateral amputation following non-union of fractures of both tibiae.

This patient had three sets of pylons provided, each set raising him about 7 in. Right pylon provided with hinge. (Hinge was below level of patient's own knee.) *Right pylon* weighed 4½ lb. with knee mechanism. *Left pylon* weighed 3 lb. with knee mechanism.

He was able to return to work as a telephone operator.

FIG. 11a.—Splint used for treatment of fractures of fifth metacarpal.

FIG. 11b.—Banjo splint for treatment of radial palsy.

FIG. 9

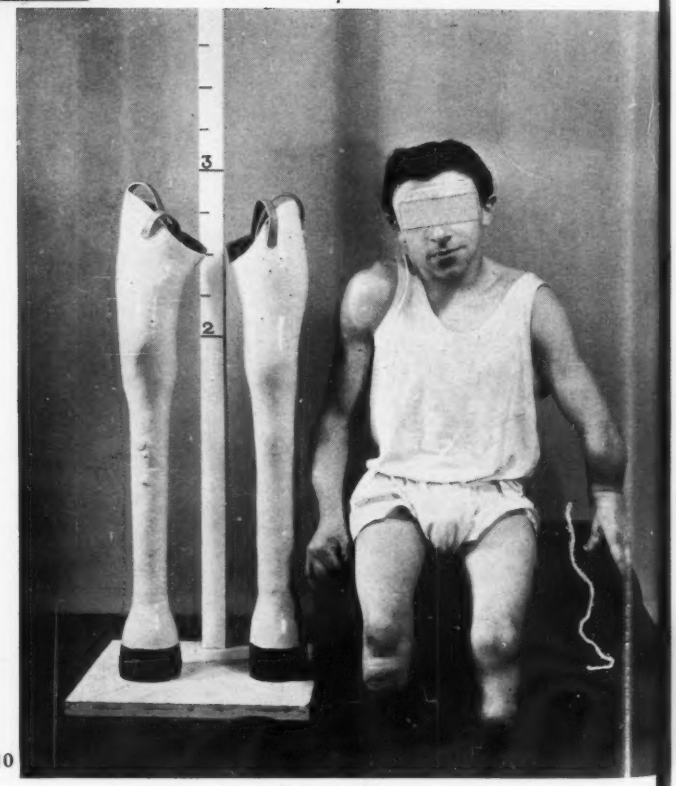

FIG. 10

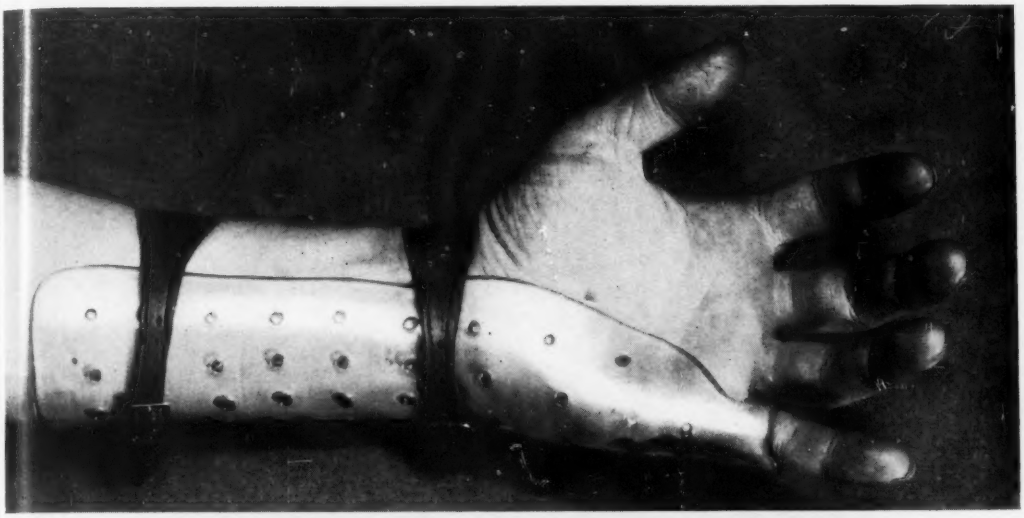

FIG. 11*a*

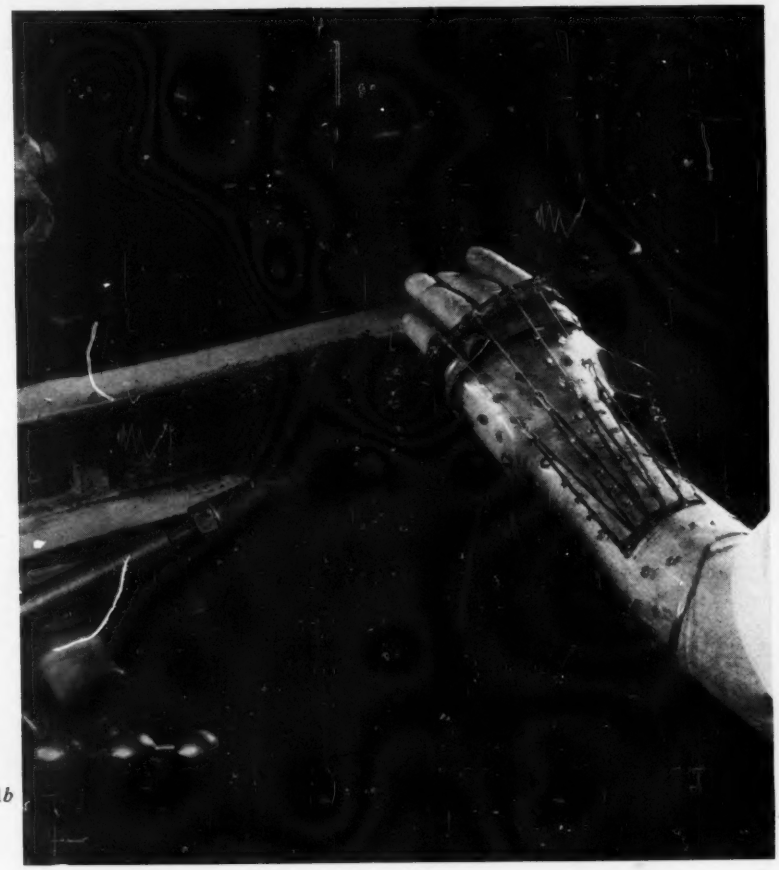

FIG. 11*b*

FIG. 11c

FIG. 11c.—Warm air box for treatment of injuries and rheumatoid conditions of the hand and wrist (used instead of wax baths). Apparatus designed to give active flexion and extension of wrist while operating machine.

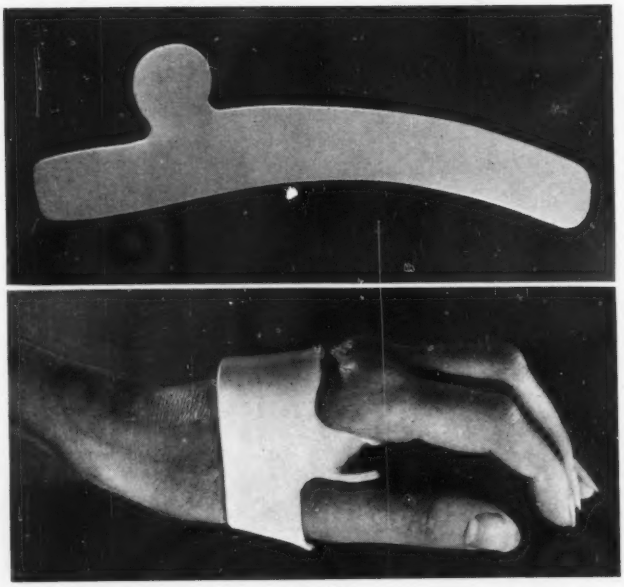

FIG. 12

FIG. 12.—Opponens paralysis splint. There is no palmar bar. Each end of the splint turns over the thena and hypothena eminences.

Figs. 11a, b, c by kind permission of Vauxhall Motors Ltd., and Fig. 12 of E. J. Nangle from "Instruments and Apparatus in Orthopaedic Surgery".

$\frac{1}{8}$ in. or $\frac{3}{16}$ in. in diameter in weight-bearing areas, otherwise small blisters may be formed. Appliances may be kept clean by washing with warm, soapy water, and are unaffected by normal body secretions or by fluids used in industry. They are light in weight, and do not distort with use. The material is dissolved by chloroform, acetone, benzene, and trichlorethylene.

Splints made from this material are most suitable for treatment of certain conditions in Group 2, particularly tenosynovitis round the wrist joint (Thompson, Plewes, and Shaw, 1951).

Where a slightly more resilient material with better fatigue resistance is required, certain grades of rigid polyvinyl chloride and co-polymers of polyvinyl chloride and acetate are useful. Fig. 12 shows a splint used in the treatment of opponens paralysis. A standard shaped blank is locally heated over a Bunsen burner and moulded free-hand to the form required. This splint holds the thumb in mid-opposition, but allows freedom of abduction and extension, the resilience of the material restoring the thumb to the correct position.

Summary

There are now available to the orthopaedic surgeon, the industrial medical officer, and the appliance manufacturer synthetic materials which can be used to produce, in many cases, more efficient lightweight appliances in less time and at lower cost than hitherto.

The choice of the material used depends on the type of appliance to be made and the facilities available for its manufacture.

The conditions of work of the patient must also be taken into consideration. With the exception of the cellulose acetate and glass bandage, there is at present no plastic material which can be applied satisfactorily direct to the patient.

I should like to thank Mr. T. Whitly, of the Medical Photographic Department of the Institute of Orthopaedics, for the photographs reproduced as Figs. 1, 2, 3, 3*a*, 4, 4*a*, 5, 6, 7, 8, 9, and 10.

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Brit. J. industr. Med., 1951, **8**, 298.

AN ENVIRONMENTAL STUDY OF THE CHROMATE INDUSTRY

BY

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The purpose of this paper is to give the results of an environmental study of the three chromate producing factories in Great Britain investigated by Bidstrup (p. 302), and to compare the results with those of Bourne and Yee (1950) in a similar study of the industry in the United States of America. The study reported in this communication was completed over a year ago, and before the work of Bourne and Yee was published. Thus it has not been possible to apply the experimental methods of these authors and so improve the comparison of the two studies.

Manufacture and Properties of some Common Compounds of Chromium

Chromium compounds are of considerable importance to industry, and according to Thorpe and Whiteley (1946a) Great Britain produces more than 10,000 tons of potassium dichromate per annum. The main step in the manufacture of the various chromium compounds involves the conversion of the water insoluble ore, chromite, into a water soluble chromate. The process generally adopted is essentially similar to that described by Partington (1946).

Finely ground chromite ($FeOCr_2O_3$) is intimately mixed with sodium carbonate and crude calcium carbonate (as dolomite or limestone). The mixture is conveyed to a rotating furnace where it is roasted. A series of chemical reactions occur which are probably represented by the following equations :

(1) $4\,(FeOCr_2O_3) + 4\,Na_2CO_3 = 4\,Na_2Cr_2O_4 + 4\,FeO + 4\,CO_2$

(2) $4\,Na_2Cr_2O_4 + 4\,Na_2CO_3 + 6O_2 = 8\,Na_2CrO_4 + 4\,CO_2$

$4\,FeO + O_2 = 2\,Fe_2O_3$

The calcium carbonate is added to increase the heat of the reaction. Although some calcium chromate is formed during the process, this is mostly decomposed by excess soda. The red hot product of roasting, frit, is transferred to wash tanks where hot water is carefully added. This "flooding" gives rise to a strongly exothermic reaction. As a result, the soluble sodium monochromate is leached out, and the liquor run off and is treated according to special requirements.

In order to obtain the dichromate, the monochromate liquor is treated with dilute sulphuric acid in special tanks. The reaction proceeds as in equation (4).

(4) $2\,Na_2CrO_4 + H_2SO_4 = Na_2SO_4 + Na_2Cr_2O_7 + H_2O$

The sodium sulphate is less soluble than the dichromate and much of it separates out. This is removed and the mother liquor concentrated. More sodium sulphate separates and is removed. The final mother liquor contains the dichromate which crystallises out on concentration. In order to obtain potassium dichromate a concentrated solution of a potassium salt (e.g. potassium chloride) is added to a concentrated solution of sodium dichromate. Potassium dichromate is precipitated immediately. Another important chromium compound, chromic acid (CrO_3), is prepared by adding strong sulphuric acid to a concentrated solution of potassium dichromate. Deep scarlet crystals of the acid are formed. The reaction proceeds as shown in equation (5).

(5) $K_2Cr_2O_7 + H_2SO_4 = K_2SO_4 + H_2O + 2CrO_3$

Partial drying of the principal products, namely, potassium and sodium mono- and dichromates, is carried out in filter presses and the process completed in centrifugal dryers or heated baths.

The chief compounds which are manufactured are the chromates and dichromates of sodium and potassium and also chromic acid.

The Nature of Atmosphere Contaminants in a Chromate Factory

A preliminary survey of the factories and their processes indicated that the atmosphere contaminants were likely to be particulate. Only in certain

processes, such as feeding chromate liquors into tanks, or flooding frit in the extraction tanks, were chromium compounds likely to be encountered in droplet or spray form. All the principal reactants contributed to the factory atmosphere. These contaminants varied in proportion and included the following: (*a*) chromite ore; (*b*) sodium carbonate; (*c*) calcium carbonate (as dolomite or limestone) all of which were in the crude form and well mixed before feeding into the roasting furnace; (*d*) products of the various interactions of (*a*) and (*b*) as indicated by equations 1–3; (*e*) monochromates, either sodium or potassium; (*f*) dichromates, either sodium or potassium; (*g*) miscellaneous dusts with compositions depending on the other processes in the factory, for example, chromic acid and chrome tan.

Chromite appeared to be the principal insoluble substance, although calcium carbonate and some of the products of the roasting process such as Fe_2O_3, FeO, magnesia, and silica contributed to this fraction. The amount of free silica was unlikely to be high, as most samples of chromite are said to contain less than 6% and many less than 2% (Thorpe and Whiteley, 1946b). The other products of the reactions were soluble.

Interconversion of Monochromate and Dichromate

The wide range of atmosphere contaminants listed in the previous section indicated that it might be necessary to attempt a quantitative separation of the soluble salts of chromium. A further argument in favour of taking this step was the suggestion that the monochromate ion might cause lung cancer (Machle and Gregorious, 1948). However, consideration of the factors influencing the interconversion of mono- and dichromates led to the conclusion that such a separation, particularly of factory atmosphere contaminants, would be impracticable if not impossible.

The interconversion of mono- and dichromates is illustrated by the simplified equilibrium equation (6) where B is a base e.g., sodium or potassium.

(6) $B_2Cr_2O_7 \rightleftharpoons B_2CrO_4 + CrO_3$

Dichromate (Orange)		Monochromate (Yellow)
Dilution	→ ←	Concentration
Alkalinity	→ ←	Acidity
Cold	→ ←	Heat

Two of the chief factors influencing this equilibrium are *p*H and dilution. Thus a shift in *p*H towards the acid side will favour the formation of dichromate ions; this is used in the manufacture of bichromate. On the other hand alkalinity will favour the monochromate. Dilution of a solution of a dichromate increases the amount of monochromate. Concentration of a solution of a monochromate shifts the equilibrium in favour of the dichromate.

According to Dehn (1914) concentrated solutions contain, in addition to mono- and dichromate, tri- and even tetrachromate ions, whereas in very dilute solutions possibly of the order of 0·003% or less, only chromate ions are present. Other authors have expressed similar views, for example Mellor (1930).

Bourne and Yee (1950) have demonstrated that rafter and air-borne dust samples are predominantly alkaline. Although no *p*H measurements were made on samples from British factories, many of them were heavily contaminated with sodium carbonate and must have been alkaline.

Furthermore, many of the samples from the British factories were taken in steam filled atmospheres, e.g., near wash tanks during flooding, and by centrifugal dryers, thus adding to the moisture content of the air-borne particles and therefore increasing the dilution.

It was concluded from these observations that moist air-borne particles would contain variable mixtures of mono- and dichromates, but that the tendency would be for the equilibrium to be balanced in favour of the monochromate ion.

Although Martin, Hixson, and McNabb (1948) have described a good method for estimating mono- and dichromate ions in each other's presence in concentrated solutions by a spectrophotometric technique, it was felt that this method would not be applicable to the survey, particularly as no method could be found of preserving the monochromate-dichromate equilibrium for trapped particles or droplets.

These considerations led to the decision to estimate only mass concentrations of total insoluble and total soluble chromium compounds.

Although the same general principles of the manufacturing process applied in each of the three factories, the lay-out of the works varied slightly, and there were differences in the types of equipment used. The concentration of contaminants in the atmosphere varied because the factories were roofed and not completely walled. This allowed changes in the weather, speed and direction of the wind, and relative humidity, to affect conditions in the working atmosphere and made accurate comparisons of the environmental conditions in the three factories impossible.

Experimental Methods

Sampling.—Atmosphere samples were taken at points near each stage in the process, and having regard to the differences in the lay-out of the works, at comparable points in each factory. The positions of these sampling points are given in Table 1. Except where an obvious change in the concentration of atmosphere contaminants occurred, as in the vicinity of the drying cubicles, single (grab) estimations were made at all points. Air samples

from 1 to 10 cu.m. in volume were collected over periods of time varying from half to five hours.

Two general methods were employed in trapping atmosphere contaminants. They were collected in dilute aqueous alkali after passage through the jet of an impinger acting as a critical orifice or on dry Pyrene filters.

Treatment of Samples and Analytical Methods.—By means of the two methods described in the previous paragraph samples, either soluble or insoluble in alkali, were collected. In order to convert it into a soluble form, the insoluble material was separated from the liquid in the impinger flask by centrifuging, and fused with excess sodium carbonate at 800°C for two hours. Pyrene filters were washed with dilute alkali to remove the soluble compounds and the residue, containing chromite and other insoluble matter, was treated in the same way as the insoluble material in the impinger flask. Estimations of chromate were carried out using the standard diphenyl carbazide method (Jacobs, 1941). Bourne and Yee (1950) used filter paper for the collection of their samples and then analysed them for trapped chromium by a polarographic technique devised by Urone, Druschel, and Anders (1950a). This method is stated to have a sensitivity of the order of 0·02 μg./ml. Scott (1939) states that at least 0·0001 mg. of chromium may be detected by the use of diphenyl carbazide, and more recently Urone, Druschel, and Anders (1950b) have employed this reagent to estimate 0·005 μg. of chromium in atmosphere samples and mists. It is considered that the polarographic and colorimetric methods are sufficiently specific and accurate to permit reasonable comparisons to be made between the two studies.

Results

Detailed results are set out in Table 1. For the purpose of presentation the process is divided into phases, and it will be seen that there is wide variation in the concentrations of the soluble and insoluble compounds of chromium. The principal features are that during mixing of the reactants, phase 1, the

TABLE 1

COMPARISON OF AVERAGE CONCENTRATIONS OF CHROMIUM IN BRITISH AND AMERICAN CHROMATE FACTORIES

Phase in Process No.	General Description	Details of Sampling Points	British (Concentrations in mg. Cr./cu.m.)				Total	Cr^{+3}:Cr^{+6}	American (Concentrations in mg. Cr./cu.m.)			
			Cr^{+3} Average	Range	Cr^{+6} Average	Range			Cr^{+3}	Cr^{+6}	Total	Cr^{+3}:Cr^{+6}
1	Pre-reaction phase: mainly insoluble chromium (chromite) (lime and ash)	Near mixers only	2·14 (3)	3·27–0·818	0·005 (3)	0·01–0·002	2·145	430:1	1·52 1·2	0·03 0·1	1·55 1·3	6:1 (6)
2	Reaction phase: conversion of insoluble chromite to soluble chromate (roast)	Discharge end of furnace; by frit hopper during discharge; by wash tanks during emptying of frit	0·17 (9)	0·660–0·0033	0·029(10)	0·146–0·0005	0·199	5·8:1	0·26	0·39	0·65	2:1 (62)
3	Reaction phase continued: extraction (filtering)	By wash tanks before, during and after flooding; digging out of extracted frit; running off monochromate liquor	0·037 (6)	0·214–0·0009	0·52 (10)	4·15–0·0005	0·557	1:14	0·08	0·12	0·2	2:1 (10)
4	Formation of dichromate (liquor)	By acidifier tanks	0·014 (7)	0·094–0·0002	0·056 (8)	0·175–0·005	0·070	1:4	0·09	0·09	0·18	2:1 (12)
5	Concentration phase and drying of soluble chromates (shipping)	By centrifugal dryers inside and outside cubicles; by evaporating pans	0·0053(7)	0·019–0·00056	0·88 (11)	5·68–0·0004	0·8853	1:166	0·3	0·2	0·5	8:1 (3)
6	Packing of dry purified soluble chromate (shipping)	By mechanical chromate filler; by men filling drums manually	0·0009(3)	0·0022–0·0003	0·467 (5)	0·92–0·051	0·4679	1:519	—	—	—	—
7	Miscellaneous processes in addition to main ones; for example:											
	(1) Chromic acid		0·036 (3)	0·106–0·0015	0·087 (3)	0·142–0·034	0·123	1:2·1	—	—	—	—
	(2) Milling chrome sulphate		0·5 (1)	0·5	0·003 (1)	0·003	0·503	166:1	—	—	—	—
	(3) Mixing dichrome and sulphur		—	—	17·0(1)(?)	17·0 (?)	17·0	—	—	—	—	—
	(4) Milling chrome oxide		·0006 (1)	0·0006–0·005	0·005 (1)	0·005	0·0056	1:8	—	—	—	—
	(5) Chrome tan		—	—	0·003 (1)	0·003	0·003	—	—	—	—	—
	(6) Waste hopper		0·170 (1)	0·170	0·002 (1)	0·002	0·172	85:1	—	—	—	—

A dash (—) indicates that no values are available. Figures in brackets indicate the number of samples. The equivalent name of the American process (Bourne and Yee, 1950) is placed in brackets after the descriptions of the phases. Approximate American figures are calculated from diagram 1 in the paper by Bourne and Yee (1950).

insoluble form Cr^{+3} is far in excess of the soluble, Cr^{+6}, whereas in the drying and packing, phases 5 and 6, the reverse applies. The average concentrations of chromium in the atmospheres of British and American factories are based on 96 representative samples from the factories of Great Britain, and 121 from those in the United States of America.

Discussion

The wide range of many of the British values, e.g., in reaction phase 2, suggests the influence of variable ventilation since the processes were similar and continuous, and sampling points placed at comparable points in the three factories. The scatter is not so marked in the American figures. This could be due to greater control of ventilation near each plant in the process, but no definite information is available on this point.

It is obvious that there is some danger in making absolute comparisons between British and American figures, particularly as the samples were grabs in both cases. At best it can be said that the British figures, and probably the American, represent values likely to be encountered during average working periods.

Elkins (1950) states that the maximum allowable concentration of Cr as CrO_3 is 0·1 mg./cu.m. This is equivalent to 0·048 mg. Cr/cu.m. Many of the values recorded in the British and American figures are much higher than this, and although perforation of the nasal septum appeared to be common among many of the British workers, there was no unduly high incidence of lung cancer (Bidstrup, page 302).

Industrial hazards due to chromium are usually attributed to water soluble derivatives of hexavalent (Cr^{+6}) chromic acid. There are chromic acid itself and the mono- and dichromates. It is commonly stated that solubility in water is an important property in determining the toxicity of these compounds (Elkins, 1950). For example, lead and zinc chromate are stated to be less toxic than the corresponding sodium and potassium salts. However, in view of the lack of any information to the contrary, it is felt that the insoluble trivalent (Cr^{+3}) forms such as chromite cannot be arbitrarily defined as " safe " compounds. Therefore it seems reasonable to suggest that the most dangerous points in the manufacture of chromate will be those which produce the highest levels of insoluble and soluble chromium compounds. In the factories studied, these points were to be found at the pre-reaction phase where the insoluble chromium reached a maximum value of 3·27 mg./cu.m. and the drying phase where the soluble form reached the level of 5·6 mg./cu.m.

Men working at these points wore adequate dust masks and were not continuously exposed to the highest concentrations. The mixers were situated in fairly open areas of the factory and were well ventilated. The centrifugal dryers were housed in small cubicles more or less protected from draught. They were also isolated from the general atmosphere of the factory.

During the process of drying, which lasted from two to three hours, the workman was not present in the drying cubicle for more than a few minutes. His main functions were charging the dryer, keeping watch to see that it was working properly, and finally emptying it before the packing of the finished product. In the early stages of drying the hazard was relatively low if measured by atmosphere levels of chromium, but these increased rapidly to the higher values after two to three hours.

Summary

A survey has been made of the contamination of the atmosphere by soluble and insoluble chromium compounds in the three factories in Great Britain making basic chromates from the ore, chromite. The results are compared with those obtained in a similar survey in the United States of America.

The maximum concentrations of both soluble and insoluble forms of chromium in the atmospheres of factories in Great Britain are greater than those found in the factory in the United States of America, and the minimum concentrations are lower. The main point of similarity is the very high ratio of Cr^{+3} to Cr^{+6} in the ore mixing stage.

The authors wish to express their thanks to the management in each of the chromate producing factories for their cooperation and hospitality. They also wish to thank Dr. Donald Hunter for his help and encouragement, Dr. P. Lesley Bidstrup for many helpful discussions, and Messrs. E. King, P. N. Casbolt, A. J. Hobbs, and Mrs. S. Cox for technical assistance.

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Brit. J. industr. Med., 1951, **8**, 302

CARCINOMA OF THE LUNG IN CHROMATE WORKERS*

BY

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In a review of the literature on carcinoma of the respiratory system occurring in persons exposed in their work to chromates Baetjer (1950) found 122 recorded cases. Of these 109 worked in the chromate-producing industry, 11 in the manufacture of chrome pigments, and two in other industries where chromium compounds are used. Sixty-three of the cases occurred in Germany, 57 in the United States of America, one in Switzerland, and one in Great Britain. In the majority the primary growth was in the lung. The case reported from Great Britain by Newman (1890) was one of adreno-carcinoma of the nares in a chrome worker aged 47. The septum of his nose had become perforated 20 years previously, and the patient stated that many of his fellow-workmen were similarly affected. In his description of the findings in this case Newman emphasizes that the nasal septum was not involved in the carcinomatous change. He states: "... on examination a large rounded perforation was seen in the nasal septum, large enough to allow a shilling to pass from one nostril to the other. The margins of the perforation were smooth, completely cicatrized, pale in colour and free from ulceration. The anterior margin of the perforation is situated about half an inch from the top of the nose. . . . The tumour occupied the anterior half of the left nostril and almost touched the septum. It was firmly attached to the inferior turbinate and caused some displacement of the nasal bones". Legge (1922) reported that he could find no evidence of epitheliomatous change in 175 cases of chrome ulceration.

Machle and Gregorius (1948) studied the causes of death among workers in the chromate-producing industry in the United States of America. They concluded that the proportion of deaths due to carcinoma of the respiratory system was 16 times the expected proportion. The crude death rate for carcinoma of the lung was 25 times the normal. Baetjer (1950) confirmed these findings for the industry in the United States of America in a study based on the records from two Baltimore hospitals, each of them near a chromate-producing factory. Since neither mortality data nor reliable information regarding former employees were available for any of the three factories making basic chromates from the ore chromite in Great Britain, a search for cases of carcinoma of the lung was made among workers employed in the industry in 1949. Although this was the only method of investigation which could be adopted in the circumstances, it has the limitation that no definite conclusions as to the incidence of carcinoma of the lung in chromate workers in Great Britain can be drawn from the findings unless these are confirmed in a follow-up study.

Method of Investigation

Seven hundred and twenty-four workers were interviewed and radiographs of the chest were taken on 14 × 17 in. films. In addition, 31 workers were interviewed but not radiographed. Works lists furnished before the survey began gave the names of 588 employees. In addition, 198 workmen whose names were not included in the original works lists, but who were employed on the manufacture of basic chromate, attended for *x*-ray examination, making the total number of workmen at risk 786. Twenty-one of these had left the works before the survey began, and four were sick during the survey. The total number of workmen exposed to chromium compounds in these factories at the time of the survey was therefore 765. Six men declined both interview and *x*-ray examination (Table 1).

The investigation included a personal interview with each employee at his place of work. Present and past occupations were recorded together with a clinical history which included specific enquiry for symptoms such as cough, dyspnoea, and pain in the chest. In persons in whom the clinical history or general appearance was suggestive of ill-health, and in all cases where an abnormality was detected in the radiograph of the chest, a complete clinical examination was made. The

* Report of an investigation in the chromate-producing industry in Great Britain.

TABLE 1

CLINICAL AND RADIOGRAPHIC SURVEY OF WORKERS IN THE CHROMATE-PRODUCING INDUSTRY IN GREAT BRITAIN

Works list		588	786
Workmen at risk radiographed but not on original works list		198	
Workmen interviewed and radiographed	724	755	
Workmen interviewed, but not radiographed	31		
Workmen left before survey began	21		786
Workmen sick during survey:			
sprained ankle	1		
sciatica	1		
cardiac failure	1	4	31
reason unknown	1		
Workmen refused examination	6		

films were read by two physicians, and each film was looked at on two occasions at an interval of at least one week. In doubtful cases the opinion of a radiologist was obtained and findings confirmed by further investigation. Environmental conditions were investigated in each factory to determine the possible exposure to chromium compounds in the various jobs in the process. The results of the environmental study are reported in an accompanying paper by Buckell and Harvey.

Description of the Process

Metallic chromium and the chromium compounds used in industry are obtained from the basic chromates, sodium and potassium dichromate or monochromate. These compounds are prepared from the ferrous ore, chromite or chrome ironstone $FeO\ Cr_2O_3$. The ore contains from 40 to 50% of chromium, and alumina and silica are present as impurities. The ore is dried, crushed, mixed with limestone and the carbonate either of sodium or of potassium, and heated in a rotary furnace for eight hours at a temperature of 1200° C. In many factories throughout the world the introduction of rotary furnaces to replace reverbatory furnaces has taken place only in the last decade. The oxide is converted to monochromate, and the frit from the furnace is carried to washing or leaching tanks arranged in series. The monochromate is dissolved out by repeated washings with water, and the concentrated liquor containing monochromate is treated with sulphuric acid. Dichromate is formed by double decomposition and sodium sulphate is a by-product. The process is the same in the three factories in Great Britain, but there are differences in the lay-out of the works and in the type of equipment. In most factories in the United States of America and in Germany roasting of the ore is done in two stages. In the second stage residue from the leaching tanks is dried and crushed and used as a filler in place of limestone. This residue contains as much as 1% of monochromate. In the factories in Great Britain the residue from the leaching tanks is discarded in a moist condition and carried to dumps outside the factory.

Buckell and Harvey (q.v.) report the results of the sampling of atmosphere in chromate-producing factories in Great Britain, and compare the findings with those recorded in a factory in the United States of America by Bourne and Yee in 1950. Concentrations of both soluble and insoluble chromates were found to be much higher in the atmosphere of the factories in Great Britain than in the factory studied by Bourne and Yee.

Results of Clinical Investigation

Three hundred and six of the 724 workmen examined were over the age of 44, and of these 131 were more than 60 years of age. The average age was 44·3 years (Table 2). It is the custom in all three factories for employees to work on different stages of the process from time to time. This fact and the conditions in the factory due to variations in ventilation, temperature, and humidity make it impossible to assess the exposure to chromates of individual workmen. Two hundred and thirty-seven of the 724 persons examined had been employed in the chromate-producing industry for more than 15 years; of these, 165 had worked in the industry for more than 20 years. The average duration of exposure to soluble and insoluble chromates in the working atmosphere was 12·2 years (Table 3).

One case of carcinoma of the lung was found among the 724 workers interviewed and radiographed. This occurred in a man aged 59 who was interviewed on August 22, 1949. He had been employed as a process worker on the manufacture of bichromate of ammonia for eight months. Twenty years previously he had worked in the crystal-house in the same factory for six years. He had experienced chrome ulceration of the skin on both occasions. At the interview he complained of dyspepsia including flatulence and loss of appetite. He had been treated in the past for duodenal ulcer. Although all workers who were interviewed were asked particularly about such symptoms as cough, dyspnoea, and pain in the chest, this man complained of no symptoms suggesting disease of the respiratory system. He weighed 9 st. 12 lb., and he stated that this was his usual weight. A radiograph of the chest on September 14, 1949, revealed enlargement of the hilar shadow on the right side, and a diagnosis of carcinoma of the lung was made at

TABLE 2
ANALYSIS INTO AGE GROUPS

Age in Years	Number of Workmen
15–	45
25–	151
35–	219
45–	175
60 and over	131
age unknown	3

Average age = 44·3 years
Number of workmen over 44 years = 306

TABLE 3
DURATION OF EXPOSURE TO CHROMATES

Years	Number of Workmen
Less than one	82
1–4	211
5–9	110
10–14	84
15–19	72
20–24	41
25–29	41
30–34	35
35–39	21
40–44	13
45–49	9
50 and over	5

Average duration of exposure = 12·2 years
More than 15 years in chromate-producing industry = 237
More than 20 years in chromate-producing industry = 165

this time. He was admitted to hospital on November 26, 1949, and died shortly after admission. At necropsy, carcinoma of the bronchus to the right upper lobe with secondary deposits in the lung, mediastinal glands, liver, and vertebrae were found. In addition there was a chronic pyloric ulcer which had perforated causing acute general peritonitis. The history of this man's terminal illness was obtained from a brother. The patient had been ill for 11 weeks before being admitted to hospital on the day of his death. He complained only of pain in the back, and thought he had strained his back at work. There was a striking loss of weight from 9 st. 12 lb. in August to 8 st. 4 lb. at the time of his death three months later.

Active pulmonary tuberculosis was found in 17 of the 724 workmen radiographed, and healed lesions in the lung parenchyma in four. One case of mitral stenosis with venous congestion of the lungs, and one of dextrocardia were revealed. A man aged 71, who had worked in the industry for 35 years, died from heart failure during the survey. There is no reason to believe that death was due to disease of the respiratory system.

A follow-up enquiry by letter 13 months after the survey was completed disclosed that four workmen who had taken part in the investigation had died. In one of these death was due to carcinoma of the lung. An attempt is being made to observe for a further period of two years the incidence of carcinoma of the respiratory system among the workmen examined in 1949.

Discussion

Kennaway and Kennaway (1947) record that the incidence of carcinoma of the lung in men in England and Wales between the years 1921 and 1945 has increased sixteenfold. They were unable to find any particular occupation among 63 studied to which this increase could be attributed. The sources of error in statistical work based on a study of death certificates are discussed, and include the large sampling error which is inevitable when small numbers of men are employed in a particular occupation. Relatively few men are engaged in the chromate-producing industry, and it may be difficult to prove by statistical methods that the incidence among them of a common disease such as carcinoma of the lung is abnormally high (Bidstrup, 1950).

Examination by mass radiography of 724 employees in the chromate-producing industry in Great Britain revealed only one case of lung carcinoma. This observation may be compared with the results obtained among men in Great Britain in 1949 by mass radiography units of the Ministry of Health. The criteria of diagnosis adopted in this survey are not necessarily the same, nor can the mass radiography units be assumed to have examined an entirely representative cross-section of the population. In spite of these factors, the comparison should provide an approximate indication of the normality of the experience in the chromate-producing industry. Table 4 shows the morbidity rates due to intrathoracic new growths at different ages as determined by the national mass radiography units, and the number of cases of intrathoracic new growths which might therefore have been expected. From Table 4 it is seen that 0·41 cases were expected, whereas, in fact, one was found.

The numbers are clearly too small for any definite conclusions to be drawn from the results of this investigation. The same result could have been obtained whether workers employed in the chromate-producing industry were at particular risk of developing lung carcinoma or not. It is unlikely that the risk would be as great as 25 times the normal as is stated by Machle and Gregorius

TABLE 4

MORBIDITY RATES AT VARIOUS AGES

Age in Years	Incidence of Intrathoracic * Malignant Disease in Males in Great Britain	Expected Incidence of Intrathoracic Malignant Disease in 724 workers in the Chromate-producing Industry in Great Britain
15–	0	0·0
25–	2	0·003
35–	16	0·035
45–	76	0·133
60 and over	186	0·243
All ages	—	0·414

* Figures obtained from Mass Radiography Report (1949) by permission of Dr. Norman Smith and Dr. Peter Kerley, of the Ministry of Health (rate per 100,000).

(1948) to be the case for workers in this industry in the United States of America.

The hazard would be better assessed by the follow-up over several years of persons at risk, and the comparison of the number of deaths among them due to lung carcinoma with the number expected from the national mortality rates. Table 5 shows the death rates from carcinoma of the lung at different ages as given by the Registrar-General for 1948. The figures for 1949, the year in which the survey was carried out, are not yet available. The number of deaths expected to occur in one year in the population surveyed is also shown in Table 5, and it is seen that 0·44 were expected whereas one occurred. The second death from lung carcinoma among chromate workers examined occurred more than one year after the survey was concluded. The figures are again too small for definite conclusions to be drawn, but it is hoped that a follow-up study over several years will provide data from which the true incidence of carcinoma of the lung in workmen in the chromate-producing industry in Great Britain may be assessed.

Summary and Conclusions

The results of clinical and *x*-ray examination of workmen employed in the chromate-producing industry in Great Britain are reported.

The processing of chromate in Great Britain is briefly described, and reference made to the environmental study of the chromate industry by Buckell and Harvey.

One case of pulmonary carcinoma was found on examination by mass radiography of 724 workmen. The total number of workmen exposed to chromates in the chromate-producing industry was not more than 765 at the time that the survey was made.

TABLE 5

CARCINOMA DEATH RATES AS GIVEN BY THE REGISTRAR-GENERAL IN 1948

Age	Death Rate for Lung Carcinoma in Males in England and Wales, 1948 (Rate per 100,000)	Expected Death Rate for Lung Carcinoma in 724 Workmen in Chromate-producing Industry in One Year (1949)
15–	0·95	0·000
25–	3·43	0·005
35–	16·81	0·037
45–	93·33	0·163
60–69*	177·58	0·233
All ages	—	0·438

* The age group 60–69 includes all men over 60 years of age. Twenty-four of them were over 70 years of age.

The findings are compared with the incidence of intrathoracic new growth among men in the general population in Great Britain obtained by mass radiography units in 1949, and with the death rates from lung carcinoma at different ages as given by the Registrar-General for 1948.

It is not possible to assess from this investigation the true incidence of carcinoma of the respiratory system among workmen in the chromate-producing industry in Great Britain, but the results suggest that the crude death rate is unlikely to be as great as 25 times the normal.

Since it is possible that there is some increase in the incidence of carcinoma of the lung in workmen employed in this industry in Great Britain, an attempt is being made to follow for a further period of two years the health of men who took part in the investigation in 1949.

Without the cooperation of the management in each of the chromate-producing factories this investigation would not have been possible.

I am indebted to Dr. Richard Doll for assistance in assessing the results of the survey, to Dr. P. B. S. Fowler for seeing with me all the radiographs, and to Dr. Donald Hunter for advice and criticism in carrying out the investigation. Dr. Norman Smith and Dr. Peter Kerley of the Ministry of Health have made available the data on the incidence of carcinoma of the lung which is used for comparison in Table 4. Messrs. H. T. Ferrier and J. Maclagan arranged the *x*-ray examinations.

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BOOK REVIEWS

The Changing Culture of a Factory : A Study of Authority and Partici ıtion in an Industrial Setting. By Elliott Jaques, with an introduction by A. T. M. Wilson. 1951. London : Tavistock Publications, Ltd., in collaboration with Routledge & Kegan Paul, Ltd. Pp. XVII+341, 16 text figures. Price 28*s*.

The Changing Culture of a Factory is an account of a study which the Tavistock Institute of Human Relations undertook at the Glacier Metal Company's factory in West London between April, 1948 and November, 1950. Dr. Elliott Jaques who led the research team appears as the author of the book which " has been the result of the closest collaboration between myself, my colleagues . . and members of the Glacier Metal Company ". It is good to find that such a study can be published with the assent of all concerned.

Part I outlines the development of the Institute's plans for the study, and gives also an account of the Company from its founding in 1898, together with a sketch of its organization in 1947 when the Managing Director first approached the Institute. " The design chosen for the project was to collaborate with one firm which would be willing and interested to study and develop its methods for creating satisfactory group relations." Thus the focus of the study—relations *within* different groups in the factory and *between* those groups—coincided with the chief means for obtaining information, the group discussion, a technique which the Institute (and the Clinic from which it derives) has developed, and for which it is well known.

Before introducing the research team into the factory, the Institute took considerable care to obtain the consent both of the management and the elected Works Committee, and in addition they sought " cover " from the Trades Unions concerned. They were at particular pains to build up the independence of the team, so that it might avoid the appearance of taking sides—to guard the research team (as they put it) against " becoming involved in stresses between groups in the factory, and to establish from the beginning that a part of the approach used by the team would be the avoidance of capture by any particular group " in the factory. Further, the team laid down that any comments or interpretations that it might offer to any group during the course of the study would be limited to matters appertaining to that group and to the relations existing between members of the group. Thus the possibility of bias as between one group and another would be excluded as far as possible.

The body of the book—Part II—consists of reports on five problems which the team were asked to investigate. These problems were : (1) a proposal that one department should change from piece-work to time-work ; (2) proposed changes in the form and membership of the Works Council ; (3) difficulties of the Works Committee in retaining the interests of their " constituents " during periods when no outstanding issues about pay or jobs arose ; (4) proposed changes in the form of the Superintendents' Committee (which led eventually to its dissolution) ; (5) changes in the form of the Divisional Managers' meeting (which finally became the General Managers' meeting).

In all these discussions members of the research team attended, by invitation, meetings ordinary and extraordinary, now as observers and now as consultants. When appropriate, the team supplemented these group discussions by private interviews with members of the groups to obtain their views on particular issues. Despite many difficulties, the research team obtained a considerable body of information about the life of the factory, especially the way it was managed, and about the methods of joint consultation.

In Part III, following a chapter on definitions (" social structure ", " role ", " role relationships ", " culture ", " personality "), which contrives to echo and paraphrase many recent considerations of these notions without actually quoting any of them, Dr. Jaques discusses what he presumably regards as the three central processes of factory organization : (1) the sanctioning of authority, (2) the operation of authority (the executive system), and (3) social adaptation. The author does not offer any panacea or simple prescriptions for the establishment of satisfactory group relations. In the five examples described and discussed in the book, he demonstrates the important point that the *general* suspicion and anxieties of individuals and of groups are liable to become attached to *particular* practical issues and difficulties, so much so that the resolution of these practical, and maybe trivial, difficulties is thereby seriously obstructed. Indeed, such *symptomatic* difficulties are often retained as the lesser of two evils, as a device for avoiding *deeper*, more threatening troubles and issues between individuals and groups which may be unrecognized. To tackle these underlying conflicts, the group must have high morale and confidence in itself. There must also be an issue sufficiently troublesome and pressing to make it worthwhile for the group to make the sacrifices so often necessary for the resolution of serious conflicts. Only then, can the group bring them out into the open and deal with them. There is a hint that this can only be done satisfactorily with the patient collaboration and understanding of the consultant.

Thus the research team was asked to consider changes in the constitution of the Superintendents' Committee, which was, on the surface, a minor problem of organi-

zation. As the discussions went on, it became increasingly clear that the real source of trouble was a difficulty in communication between the superintendents and their divisional managers. This led to the committee becoming virtually a "refuge" for the superintendents, as "displaced persons in the executive system". After the superintendents had worked through their problem with the research team and a change in the organization of the factory had remedied the underlying difficulty, they were able to dispense with their committee altogether.

The existence of healthy groups, it would appear, presupposes a general setting in which continuing security has reduced the immediate fears concerning jobs and wages, and in which other policies are sufficiently advanced to permit "dangerous introspection", and to cope with the further difficulties which such introspection reveals. The willingness of this particular factory to accept the research team, the assistance they afforded it, and the actual appearance of the book now under review are signs that such a fortunate state of affairs does exist at Glacier.

One important source of stress which Dr. Jaques identified is the difficulty which individuals have in completely and correctly defining their "role" or "roles"—what they are expected to do and how they are expected to behave—and their consequent failure to act accordingly. The failure of the Managing Director for instance to realize his secondary role as General Manager of the London factory threw a considerable burden on his immediate subordinates who did not know quite how they stood.

Other, more general findings are less useful, as the following may suggest. "How far the authority of the executive system is sanctioned by investors and customers depends on the profitability and potential profitability of the concern and on the quality of its product;" "the factory must adhere to the laws of Britain and implement governmental regulations, trade agreements, negotiated wage agreements, and conditions of work;" "members of the concern having been brought up within the British culture, are unconsciously limited in the extent to which they can deviate from its traditional practices. Moreover, patterns of behaviour and organization within the concern must remain consistent with the patterns of behaviour and expectations of a community that carries this culture. . . ."

Since the director of the research team is a physician, it is disappointing to observe that there has apparently been little attempt to relate these social problems within the factory to the physical and mental health of the workers; indeed, the usual indices of industrial health and factory welfare such as accident, lateness, and sickness rates are scarcely examined at all. The only figures given show the monthly average of days lost per person through certified sickness in 1942–49; the labour turnover as an annual percentage; the numbers leaving "at company request" during the 1949 "redundancy crisis"; and the firm's financial position from 1936 to 1949—and these data are set out in diagrams from which it is difficult to read exact numbers.

In the "Operational Plan of the Project" (pp. 4–5) Dr. Jaques points out the necessity of taking into account "the larger social forces emanating from the general economic situation, the competitive position of the factory and the characteristics of the local community". In practice, however, this principle has been forgotten and the factory appears to be suspended in a social void—despite the rude incursion of an international economic blast on page 49 which caused 160 out of an average of 1296 workers to leave within six months "at the company's request". There are also very occasional references to trade unions, to the firm's social club, and to the interests of the workers in families, homes, hobbies, and other things. Surely it is accepted by now that an individual's interests and activities at work and outside it are likely to affect one another, and his own feelings about all of them—and the case is the same for the factory as a whole. No one disputes the legitimacy of limiting the questions asked in a research study to those which can be answered in the time and with the resources available, provided some estimate of the effects of the various other factors are set out and related to a definite theoretical position. If this has been done by Dr. Jaques the results do not appear in the text. The study therefore remains open to many of the criticisms made of the Mayo study at Western Electric which, incidentally, is the only work of this kind to appear in the list of references (one other is mentioned in passing). The resemblance to the Hawthorne study is increased by the apparent disregard of Dr. Jaques, like the Mayo group before him, of the considerable amount of work on industrial relations done by other people and easily available to any one interested. This work is sufficient in the U.S.A. at least to be divided between half a dozen different academic disciplines, several research institutes, and a good number of journals. It is difficult to see why Dr. Jaques apparently disregarded all this work, when by taking it into account he could have increased the value of his study and set it in the context of what is already known and what only guessed at.

This segregation (or as Dr. Jaques has called it "*maldaptive segmentation*") of the research work from the rest of life has another important aspect. The research team has studied a single factory—that is it has made a case study. To make full use of a case study it is necessary to know the extent to which the case studied is typical of all phenomena of that class; in this instance, which of the findings are applicable to most kinds of factories, which to a limited number, and which are peculiar to this particular factory. Much of the information which would enable such comparisons to be made is not presented—and what there is suggests that the factory is a most unusual one, in which what are elsewhere likely to be important and immediate problems have here been already tackled and resolved, in part at least. A further complication in this kind of study of social behaviour is that two of the principal means of getting information—the interview and the group discussion—are themselves kinds of social behaviour. The research team has tackled this latter difficulty in a remarkably ingenious and persevering way.

But in the process it has gone on to develop two points—the restriction of comment to the limited and particular group of the moment, and the independence of the research team—which surely are matters of research *tactics*, into *principles* which have guided and confined the entire study within the restricted bounds already described, and without which, its considerable value would have been still more enhanced.

It will of course be obvious that these remarks are to be taken in their context—of gratitude that here at last is a serious and indeed pioneering study of some of the least accessible features of human relations in industry.

D. H. ALLCORN

Skill and Age—An Experimental Approach. By A. T. Welford assisted by C. G. A. Allan, R. M. Belbin, Betty M. Bernadette, Ruth A. Brown, A. B. Cherno, H. Kay, Antonia Sewell, and J. Szafran. 1951. London: Oxford University Press. Pp. ix+159. Price 8*s.* 6*d.*

This book is based upon the work of the Nuffield Research Unit into Problems of Ageing during the period 1946–8. The Unit, led by Mr. Welford, has from its inception been attached to the Cambridge Psychological Laboratory, under the direction of Sir Frederic Bartlett. In a foreword the latter suggests that the Report should "be judged from two points of view: as a contribution to the fundamental psychology of human skill and of methods which make its accurate measurement or assessment possible, and as a study of the changes in skill which appear to be consequent upon increasing age". If this, however, is taken in conjunction with the opening sentence of Mr. Welford's introduction, where he says that "the studies described here have been conceived within the framework of the research on the measurement and analysis of human skill which was developed in the Cambridge Psychological Laboratory during the war", the reader is less likely to err in blaming the author for not doing what in fact he never felt obliged to do. This is not intended to be a treatise on the subject, with the Unit's findings integrated into the general body of relevant knowledge; it is a frankly Cambridge report, as evidenced by the fact that of a brief bibliography of 23 references, no less than 16 emanate from the Cambridge Laboratory.

Thus understood, the Report has considerable merit in several respects, both in content and presentation. If judged in terms of Professor Bartlett's criteria, and within the concept of the nature of skill advanced in the third chapter of the book, the work reported undoubtedly constitutes a further advance in methodology and provides a scientifically-derived corrective to several popularly-held notions about the effects of ageing. Whether one is able to agree that it also contributes significantly to what is described as "the fundamental psychology of human skill" is perhaps very much a function of the reader's use of the word "fundamental". The emphasis on the relative importance of the central mechanisms of the receptor side over that of the effectors and of the peripheral mechanisms may have already appeared to psychologically-sophisticated readers as being a likely working hypothesis. That within the honestly-stated limitations of these studies this hypothesis seems best to explain the experimental findings is, however, a step forward. The language and diagrams of the text are in general commendably clear, with one or two glaring exceptions such as the sentence at the head of p. 148: "It must be emphasised that such analysis does not involve merely the taking of several different scores relating to the same total performance, but is a true analysis in the sense that *sets* of scores, each of which accounts for *all* the data of a particular type, are taken and used *simultaneously* when assessing the experimental results" (author's italics). No doubt the author was so familiar with his material that this sentence appears to him lucid in the extreme, but this has not proved the case with the reviewer and others. This leads on to one general criticism of an otherwise valuable little book: when the subject matter is by its nature complex, even the exclusion of all mathematical statistics to an appendix and a prolific use of line diagrams does not justify such wishful thinking as that the book as a whole will be readable for labour managers and industrialists. Most of the experimental results, forming half the text, demand sustained interest and considerable concentration. Once again we are presented with a reminder that technical data of a specialist nature and conclusions therefrom which can be stated in everyday language, simply do not mix to form a smooth text for a heterogeneous public. This warning should not, however, be permitted to excuse those concerned with the industrial implications of ageing from the worthwhile task of studying this report.

ALASTAIR HERON

Occupational Factors in the Aetiology of Gastric and Duodenal Ulcers, with an Estimate of their Incidence in the General Population. By Richard Doll and F. Avery Jones, with the assistance of M. M. Buckatzsch. 1951. London: His Majesty's Stationery Office. Pp. 96. Price 2*s.* 6*d.* net.

The high frequency in the incidence of peptic ulcer justifies this investigation. An estimate in 1945, on the basis of hospital experience and national death rates, gave a figure of 1,500,000 people suffering from the disease, so it is clearly extremely important to learn as much as possible about the various factors in its aetiology.

The occupations investigated were those thought to have a particularly high or low incidence of ulcer. The former category includes lorry drivers, bus-drivers and conductors, and doctors; the latter includes clerks, labourers, and agricultural workers. A list of employees was obtained from each management, and the work of interviewing was divided into two stages. A preliminary interview was carried out by the social worker, who recorded particulars, such as sex, age, occupation, type of shift and hours of work per week, together with short clinical notes. These clinical notes enabled the medical worker to classify the cases into three categories: "no dyspepsia", "minor dyspepsia", and "major dyspepsia". Of all the cases classified as "major dyspepsia", a clinical diagnosis was made by the medical worker, and according to the results, the cases were then divided into the following groups: proved peptic

ulcer ; presumptive peptic ulcer ; other dyspepsia ; and no dyspepsia.

On this basis, the distribution of peptic ulcer in the sample of the investigation was obtained for the various occupations. The incidence of peptic ulcer for men was 6·5%, for women 1·7%.

It is impossible in a brief review to give details of all the results reached by the investigators, and we turn our attention, therefore, to the main problem of the report, that is, to the occupational factors in the aetiology of peptic ulcer. For the study of occupational differences, men were classified into 20 groups. Taking the over-all incidence of ulcer in the entire survey as a standard of comparison, the incidence in a given occupational group was compared with it. A high incidence was found among doctors, among a group of unskilled workers, and also among foremen and business executives. There was a low incidence among agricultural, and possibly among sedentary workers.

The authors were very careful in assessing the value of such significant differences, and not to ascribe them without further consideration of the occupational factors. Thus, the high incidence among doctors in the sample is explained by more refined standards of diagnosis, and in the case of unskilled workers, by ulcer subjects seeking sheltered occupations.

As in every statistical investigation based on a sample only, we must decide the extent to which the generalization of the results is permissible. In order to decide questions of this kind, the type of errors involved in the method of sampling should be understood. The authors of the report list the following four errors which may have affected the results : a lack of cooperation from the population surveyed ; a failure to interview the whole sample ; a false diagnosis at the social workers' interview ; and a false diagnosis at the medical interview.

Discussing these errors, the authors conclude that none of them is likely to have biased the results, and the reviewer's definite agreement with this conclusion is based on the figures provided by the report in this connexion.

There remains, however, as the main source of error, the fact that the sample of the population surveyed is not a random sample. This error, too, has been duly taken into account by the investigators, who repeatedly emphasize the shortcomings of the sample in this respect. They state that the sample was not representative of the general population with regard to age, sex, geographical location or occupation, and that these factors may have an influence on the incidence. The population was reasonably represented in the sample only in its social class composition, although the various occupations within these social classes were not so well represented.

In spite of the uncertainty resulting from these various errors, the authors arrived at certain general conclusions. This means, they saw fit to generalize certain sample results, and to apply them to the population as a whole. Thus they conclude that the important factors in the aetiology of gastric and of duodenal ulcers differ. Duodenal ulcers occur mainly between the ages of 20 and 64 ; the incidence is greater in men holding responsible positions ; and anxiety about work appears unduly common in duodenal ulcer subjects. In contrast, gastric ulcers are uncommon before the age of 35 ; they seem less closely related to the type of work, than to social class, for they are least frequent in the two wealthiest classes and most frequent in the poorest class. As to the general incidence, the report arrives at an estimate of 1,449,000 people suffering from peptic ulcer in England and Wales. This figure agrees with the estimate previously mentioned.

The results may, to the medical man, seem rather vague and unsatisfactory. He will tend to disparage them, if he is used to applying methods of the natural sciences, such as classification and experiment, which are designed to discover definite cause and effect relations, and differ from the statistical methods of social medicine. But a study of this type points out how medicine, as a natural science, can explore these problems further.

In view of the fact that generalization is the essence of scientific investigation, the authors of the report are quite justified in attempting such generalizations, even if these are based on their sample, which is, strictly speaking, non-representative. If work has been undertaken on a large scale in a report of this type, and the author, aware that the sample is not a random sample, refrains from all generalization, the whole undertaking would seem a great waste of effort. It is understandable that an author should hesitate to discard an investigation based on an apparently insufficient sample, or to expose himself to criticism, but the now fashionable escape from the difficulty cannot be recommended, for those who chose this way of escape frankly admit the insufficiency of the sample, and draw up a sort of legal document in which every conclusion is hedged in by qualifications in order to prevent any generalization of the sample results ; this attitude implies a mistaken conception of the purpose of scientific effort, the essence of which should always be generalization. What matters, after all, is not whether the author, like Caesar's wife, is beyond suspicion of drawing conclusions too hastily, but whether he has added anything to our knowledge of the phenomenon in question with any reasonable degree of certainty.

G. H. HERDAN

ABSTRACTS

(*This section of the* JOURNAL *is published in collaboration with the two abstracting Journals,* Abstracts of World Medicine, *and* Abstracts of World Surgery, Obstetrics, and Gynaecology, *published by the British Medical Association. The abstracts are divided into the following sections : toxicology ; industrial physiology ; industrial lung disease ; industrial skin diseases ; accidents and orthopaedic surgery ; industrial ophthalmology ; environment ; general. Not all sections will necessarily be represented in any one issue*)

INDUSTRIAL TOXICOLOGY

Drug Protection against the Lethal Action of Parathion. [In English.] SALERNO, P. R., and COON, J. M. (1950). *Arch. int. Pharmacodyn.*, **84**, 227.

Several cases of poisoning by the insecticide parathion (*p*-nitrophenyldiethyl thiophosphate), which is a potent inhibitor of cholinesterase, have been reported. In view of the effects of eserine, neostigmine, atropine, and magnesium and calcium salts in poisoning with di-*iso*-propylfluorophosphonate it was decided to investigate their possible prophylactic effects on parathion toxicity. Given by intraperitoneal injection in propylene glycol, this substance (93% pure) has an LD50 of about 5 mg. per kg. body weight in mice, rats, and cats. Previous injection of atropine of eserine increased the LD50 of parathion 8 times in mice and 4 times in cats. Atropine and neostigmine together gave better protection than atropine alone but neostigmine alone was ineffective in tolerated doses. In mice, magnesium and calcium salts did not give similar protection, but did delay death. They were, however, tested in animals given twice the LD50 of parathion and might have been more effective against smaller doses. Like neostigmine, magnesium sulphate increased the protective action of atropine. If eserine were given after parathion the two drugs acted synergistically as lethal agents.

The degree of protection afforded by eserine appears to be determined by the amount of cholinesterase reversibly bound by the drug before exposure to parathion and serving as a reservoir of enzyme whereby cholinesterase–acetylcholine action can be maintained in the presence of parathion. Survival is possible provided this amount represents 10% or more of the total. The cause of death in atropinized animals eventually succumbing to parathion poisoning is respiratory paralysis, probably due to the unopposed nicotinic action of acetylcholine on skeletal muscle. The fact that neostigmine itself has a strong nicotinic action may be the reason for its being less effective than eserine in prophylaxis against parathion poisoning.

Derek R. Wood.

Roentgenographic Changes and Urinary Fluoride Excretion among Workmen Engaged in the Manufacture of Inorganic Fluorides. LARGENT, E. J., BOVARD, P. G., and HEYROTH, F. F. (1951). *Amer. J. Roentgenol.*, **65**, 42.

In the investigation described samples of urine from 23 workmen employed in a fluoride plant were examined for fluorides, and radiographs of all the bones of 16 of them were obtained. Positive *x*-ray findings in the form of abnormally dense bones were found in 5 cases. Changes were present in the pelvis and spine in each of these, and in some the extremities were also affected. There was a definite correlation between the urinary fluoride content and the occurrence of bone changes. Such changes may be expected if the concentration of fluoride exceeds 10 mg. per litre of urine.

None of the men with positive findings complained of any disability, nor did they show any *x*-ray evidence of hyperplastic changes in the spine like those described by Roholm and Shortt in Danish and Indian workers with fluorosis. The suggestion is made that the increase in bone density may make coincidental changes due to osteoarthritis more apparent and that in consequence the part played by fluorides in causing limitation of mobility of the spine has been over-estimated by these workers.

J. A. Shiers.

Carbon Disulphide Hysteria. ANDRÉ, M. J. (1951). *Arch. Mal. prof.*, **12**, 9.

A case of chronic carbon-disulphide poisoning is described in a man of 54 who had worked as a spinner in a viscose rayon factory for 2 years. He was found to have weakness of the middle, ring, and fifth fingers of the left hand, most marked in the muscles supplied by the ulnar nerve. There were no sensory changes at this stage. A year later hypotonia of the flexor and extensor muscles of the left hand and diminished tendon reflexes in the left forearm were noted. By this time all forms of sensation in the distribution of the left ulnar nerve had nearly disappeared. A diagnosis of carbon-disulphide polyneuritis was made. Two years

later he had complete left hemi-anaesthesia and voluntary movements were no longer obtainable in the left hand and wrist, which were held in the *main d'accoucheur* position. There were frank hysterical manifestations by this time, including bouts of apnoea, followed by hyperpnoea.

The author emphasizes the difficulty of distinguishing signs of organic nervous changes from the hysterical features which are known to occur in this condition. He attaches importance to chronaxie measurements which were carried out on three occasions during this patient's illness. These showed values lower than the normal for the flexors of the left hand and fingers, and values above normal for the extensors. The differences were not markedly consistent, however. An electroencephalogram revealed no abnormality. The author concludes that although carbon-disulphide poisoning predisposes to hysterical nervous conditions, it can also give rise to a progressive polyneuritis, possibly due to the retention of carbon disulphide, or its products, in the body. He considers that chronaxie determinations are useful in detecting these organic changes.

John Pemberton.

Acute Phosphorus Poisoning in Man: a Study of 56 Cases. DIAZ-RIVERA, R. S., COLLAZO, P. J., PONS, E. R., and TORREGROSA, M. V. (1950). *Medicine, Baltimore*, **29**, 269.

Poisoning by yellow phosphorus has virtually disappeared in Britain with the introduction of less dangerous rodenticides. Puerto-Ricans, on the contrary, find it a cheap and useful suicidal agent; no fewer than 56 cases were admitted to one hospital in San Juan in a recent 3½-year period, 27 deaths ensuing. The only significant factors were the patient's age, the amount taken, and the vehicle, about 1 g. constituting a minimum lethal threshold, and a fluid vehicle (especially if alcoholic) increasing the mortality. Early vomiting or a washout within the first 5 hours much improved the prognosis.

Of the 56 patients 41 developed hepatomegaly, a dangerous early sign, within 24 hours; both this and early jaundice were directly related to the quantity of phosphorus absorbed. Circulatory collapse, haemoconcentration, oliguria, delirium, toxic psychoses, and azotaemia (developing in two-thirds of the cases) also occurred. The majority of deaths took place before the Hangar (cephalin–cholesterol) flocculation reaction became positive; liver function tests proved of little use. Hyperphosphataemia was noted in 8 cases without a fall in serum calcium level, indicating "tissue fixation of absorbed phosphorus". BAL was given to 24 patients "with poor results"; a toutine 1 : 1,000 potassium permanganate washout, together with the administration of mineral oil, was most effective in treatment. Early deaths, up to 48 hours, were from circulatory collapse ascribed to direct myocardial damage: later deaths, mostly within a week, were from a hepatorenal syndrome with jaundice and azotaemia. *Keith Simpson.*

The Porphyrins. The Significance of Porphyrins in Occupational Diseases. MCCORD, C. P. (1951). *Industr. Med. and Surg.*, **20**, 185.

INDUSTRIAL LUNG DISEASE

Silicosis and Tuberculosis among Steel Foundry Workers. ZANETTI E., and DOMPE, M. (1950). *Med. d. Lavoro.*, **41**, 321.

In steel foundries there is a high incidence of silicosis and tuberculosis, due largely to the quantity of dust present in the air when castings have to be freed from the mould. It is often necessary to use pneumatic tools to complete this process. Over 13,000 workers were studied, these being employed in 33 different works. Attempts were made to determine the incidence of silicosis and tuberculosis and to discover which processes were the most dangerous. The value of *x*-ray examinations was also assessed.

Various kinds of material are used to make moulds, many having a high proportion of silica. If the parts to be made are small, as in chain works, the fragments of the moulds, as they are detached, fall through a grill on to a conveyer by which they are returned to the moulding shop. Much dust forms in this way. Larger castings can be freed from the covering mould only by attacking the latter with heavy hammers. Hollow castings may often require scraping of the interior with small tools. Sometimes abrasive wheels are needed to clean and polish a casting and free it from adherent material. The mixing of the mould material does not involve much dust hazard, as it generally occurs in the open and the material may be wet. In general the methods of dust prevention are inadequate and the increasing use of pneumatic tools to clean the castings, though apparently unavoidable, much augments the risks.

In investigating the *x*-ray findings the authors used Vigilani's classification. Silicotic lungs were divided into five groups, a sixth showing concomitant tuberculosis. Cases of tuberculosis were divided into four groups of increasing severity. The workmen were put in one of the thirteen occupational groups, some of which are very much exposed to dust, others little exposed. The statistical estimation of the group incidence is made difficult by the changes of occupation within the industry. As was expected, the morbidity from silicosis and tuberculosis rose with length of employment. Radiographs were obtained in many cases from the industrial clinic or from the compensation office. Of 6,098 workers employed in the less hazardous jobs 493 had lung reticulation, 59 nodular silicosis, and 15 massive silicosis. Of the remaining 3,346 workers in more dangerous employment 414 had reticulation, nodular silicosis appeared in 140, massive silicosis in 62, and silico-tuberculosis in 22.

Five patients were selected for more detailed consideration; these were all men exposed to little dust. They had worked from 18 to 33 years in foundries. In 4 of them reticulation was evident and varied in degree; the bronchi showed up not by their translucency but rather because they were surrounded by opaque material. Three cases were complicated by tuberculosis. In one case the development of this complication seemed to accelerate the silicotic process. In a second group of 6 persons more exposed to dust the *x*-ray findings varied considerably. In the first 3, silicotic changes progressed

steadily but were much less rapid in development when less dusty work was begun. The next 2 persons had associated tuberculosis in active form. The last patient also had tuberculosis with silicosis but radiographic appearances changed little over a period of 3 years.

Preventive measures should include better ventilation and the separation of dusty from clean processes. Ventilating fans are often useful. All equipment not in use should be put away and water-spraying of floors and other parts should be carried out freely. Cleaning and spraying should be done outside ordinary working hours. Totally enclosed machines could be more often used in mixing materials for the moulds and the use of silicate should be cut down or stopped. Ventilation downwards is often preferable to upward aspiration. If this is associated with the free introduction of fresh air from above, the hazards are much reduced. There is much advantage in waiting until it has sufficiently cooled before removing a mould under a copious water spray, though this makes the process more lengthy and difficult, especially if pneumatic tools are used. In some works the mould is removed entirely by the use of water jets under high pressure (100 to 120 atmospheres). Pneumatic tools should have an attachment whereby the stream of dust is directed away from the operator by a rubber tube attached to the exhaust. When a furnace has to be demolished the dust hazard is very great and it is desirable to draw as much as possible downwards. Regular *x*-ray examination of personnel is needed and tuberculous subjects should be isolated. Of all persons examined 10·52% had reticulation and silicosis and 0·21% had associated tuberculosis. Tuberculous lesions were seen in 2·75%. *G. C. Pether.*

Tuberculosis among Native North African Workers Employed in the Industrial Fringe of Paris. DELAFONTAINE, P., DAMIENS, G., and DIACRE, R. (1951). *Sem. Hôp. Paris.*, **27**, 89.

In this article the authors discuss the medical and social factors contributing to the high incidence of tuberculosis among North African workers in Paris, and the clinical appearances and prognosis of the disease in these patients. In the Paris district the number of North Africans who are employed in local industries is estimated at 5% of the total population. The authors give no figures for the incidence of tuberculosis among them, but state that in one hospital one-quarter to one-third of the beds in the male tuberculosis wards are occupied by North Africans. Two main types of tuberculosis occur among these patients. One is an acute infection of the serous membranes—of the peritoneum as often as of the pleurae—and of hilar and cervical lymph nodes. The other is an ulcero-caseous pulmonary tuberculosis remarkable for the extent and gravity of the lesions. In some cases the diagnosis is uncertain, owing to negative sputum findings and inconclusive radiographs, but when such patients are kept at rest and under observation for a few months, the diagnosis of tuberculosis usually becomes more certain. The authors state that there is no racial tendency towards tuberculosis among these patients, all of whom are young men and 80% of whom are Berbers, but that the reasons for this high incidence of tuberculosis are mainly social. These North Africans, who are attracted to Paris by the prospect of high wages, are exposed to a colder climate than that to which they are accustomed, live in squalid conditions, eat insufficient food, work at heavy, unskilled labour, and send most of their wages home. They are often affected by amoebiasis and malaria.

Although the initial response to treatment, even with rest only, is good, the long-term prognosis is bad because the average North African has insufficient self-discipline and patience to continue the treatment. As long as he feels ill and is receiving active treatment, such as injections, he will remain in hospital, but as soon as he feels better he wants to leave. Many patients either take their own discharge against medical advice or have to be discharged for reasons of ward discipline. The same psychological factor operates with collapse therapy, for the North African cannot be relied upon to attend regularly for refills. Another factor is the long waiting list for sanatorium treatment; usually the delay is of several months. During this period the North African, improved by his stay in hospital, considers himself cured and either resumes work or goes back to North Africa, where he loses the benefits of the French Social Security system, and especially those benefits applying to diseases which need long-term treatment.

A. G. S. Heathcote.

Right Ventricular Hypertrophy in the Pneumoconiosis of Coalminers. THOMAS, A. J. (1951). *Brit. Heart J.*, **13**, 1.

A study was made at the United Cardiff Hospitals of the degree of right ventricular hypertrophy to be found post mortem in 50 unselected cases of coal miner's pneumoconiosis. Left and right ventricles were separated by dissection, weighed, and the ratio between them (LV/RV ratio) obtained. A significant reduction below the normal value of this ratio was found in 38 cases, indicating a high degree of right ventricular hypertrophy, the mean for the whole series being 1·16 (normal range 1·46 to 2·14). The lowest values to occur in cases in which there were massive pulmonary fibrotic lesions. In cases of massive emphysema with focal dust lesions there was much less tendency toward right ventricular hypertrophy and failure. It is suggested that the LV/RV ratio must be less than 1·00 before the electrocardiographic (ECG) pattern of right ventricular hypertrophy can be expected.

A total of 146 subjects, including 44 normal men of whom 16 were miners, were also studied with regard to the ECG changes to be found in right ventricular hypertrophy due to pulmonary disease. It is stated that reduction in amplitude of R and increase in amplitude of S in lead V6 are the most prominent changes in such cases. Claim is also made for the value of a chest lead in the 3rd interspace just above V2 in indicating early hypertrophy of the right ventricular outflow tract. Cardiographic studies of respiratory variation following an exertion test are described. It is concluded that ECG

evidence of right ventricular hypertrophy is not common in coal miner's pneumoconiosis until the disease has advanced to the stage of massive fibrosis, with infection, emphysema, and distortion. *L. W. Hale.*

ACCIDENTS and ORTHOPAEDIC SURGERY

Supraspinatus Tendinitis. A Survey of 300 Consecutive Cases Treated by Roentgen Therapy. STEEN, O. T., and MCCULLOUGH, J. A. L. (1951). *Amer. J. Roentgenol.*, **65**, 245.

Supraspinatus tendinitis, a synonym for subacromial or subdeltoid bursitis, is described as a primary degenerative process associated with a chronic inflammatory reaction involving one or more components of the tendon-capsule cuff. The authors discuss the pathogenesis and diagnosis of this incapacitating lesion and refer to the very extensive literature. An analysis is made of 300 consecutive cases treated by *x*-ray therapy. Males and females were equally affected, the average age being 50 years. The effects of *x*-ray therapy are considered to be mainly due to the induced hyperaemia, increased blood and lymph flow resulting in resorption of toxic materials, and the mobilization of antibodies. The normal course of treatment was 150 r (air) daily for 4 days, using a 10 × 10 cm. port at 50 cm. focus skin distance and 200-kV *x* rays filtered by 0·5 mm. Cu and 1 mm. Al. In acute cases some initial exacerbation of symptoms was not uncommon. An effort was made to classify the response to treatment and the authors claim either complete or almost complete remission of symptoms and signs in 83·6% of cases. The duration of these remissions is not stated, and a 39% recurrence rate is admitted after one course of treatment. No significant difference in response was noted in cases having a definite history of injury, nor was there any significant difference in those having radiological evidence of calcium deposits. One sub-group of patients, in whom previous therapy of various types had been employed, responded less favourably to *x*-ray therapy than the remainder of the series.

E. C. Easson.

ENVIRONMENT

Effect of Adding Carbon Dioxide to Inspired Air on Consciousness Time of Man at Altitude. HALL, F. G., and HALL, K. D. (1951). *Proc. Soc. exp. Biol., N.Y.*, **76**, 140.

The average duration of useful consciousness at simulated altitude was determined by the senior author's method in 9 young adults whose pulmonary ventilation was recorded photokymographically. At a simulated altitude of 30,000 feet (9,140 m.; 226 mm. Hg) average duration of useful consciousness increased to from 88 seconds to 163 seconds when a mixture containing 21% oxygen, 14% carbon dioxide, and 65% nitrogen was substituted for atmospheric air. At 35,000 feet (10,670 m.; 179 mm. Hg) a similar increase occurred, but was less pronounced when a mixture containing 21% oxygen, 19% carbon dioxide, 60% nitrogen was substituted for air. In both cases the prolongation of useful consciousness was attributable to increased ventilation.

J. E. Cotes.

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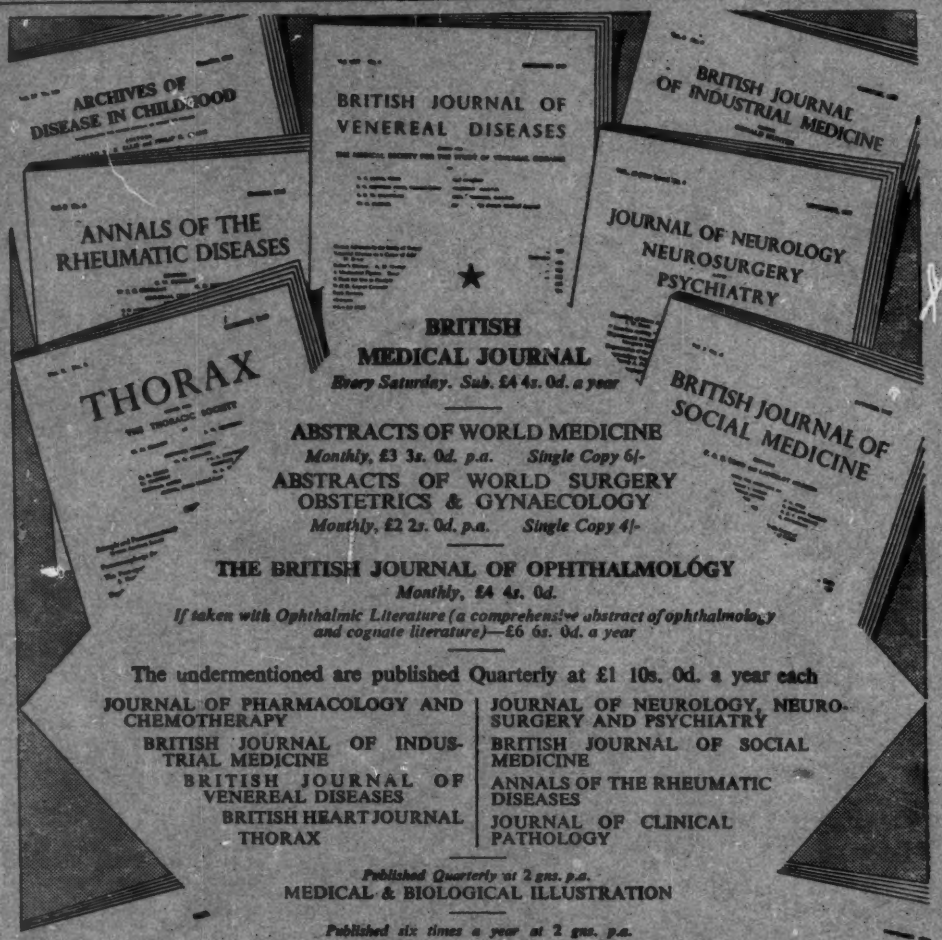
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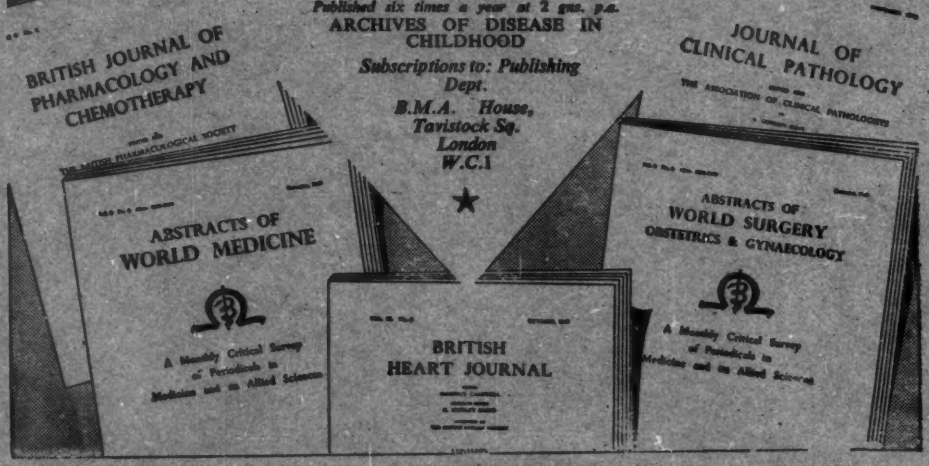
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